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RENAL NEOPLASMS: AN ENIGMA AND A CHALLENGE

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The literature enfolding the subject matter of renal neoplasms reads like a novel of romance. The differences of opinion as to the names of the tumors, the specificity of sex, their accidental, unheralded discovery, and their behavior are tantalizing. The attempt has been futile to teach medical students and house officers more than three simple facts concerning renal neoplasms: 1) That they are highly malignant; 2) that the only treatment is surgical; and 3) that the results are 20 per cent controls for a five-year period. The classifications have been confusing, the surgery not well organized, and the results discouraging. Many of the classifications are so long and complicated that it is not possible to remember them. The many references to a "nephroid" tumor imply that such a tumor is associated with the kidney but not necessarily of renal origin, and the reader is often misled as to the anatomic origin of the tumor. Furthermore, the etiology of renal tumors is still not clear. The work of Lucké in 1938 demonstrated that cancer in the kidney of the tree frog was due to a virus. Leary, in 1950, was successful in producing adenomas in the kidneys of rabbits subsequent to the development of nephrosclerosis with local implantation of cholesterol. Cabot has demonstrated conclusively that adenocarcinomas are derived from adenomas; and Kirkman and Bacon claim that renal cancers can be produced in the hamster by the use of the female hormone, stilbestrol. Such demonstrations are significant and encourage us to continue our efforts to elicit the actual cause of neoplastic activation in the kidney.

It is the author's ambition to clarify the subject of renal tumors by considering their anatomic origin and their behavior patterns in order that we may formulate a sound and logical basis for discussion. With this objective, the following classification is proposed:

CLASSIFICATION OF RENAL TUMORS

1) Nephroma (Wilms')
2) Hypernephroma, adrenal origin
3) Carcinoma of the cortex:
    a) Embryonic
    b) Adult
    c) Scirrhus—pelvis
4) Papillary:
    a) Pelvis
    b) Cortex
5) Neurogenic:
    a) Neuroblastoma

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b) Ganglioneuroma
c) Medulloblastoma
d) Schwannoma

6) Sarcoma

The kidney as an organ is a system of tubes and its physiology, though complex, is now quite well understood. From the standpoint of tumor development we may state that the kidney is composed of a capsule, epithelial tubes, a pelvis lined with transitional epithelium and a pedicle of blood vessels containing varying amounts of mesothelial tissue and nerve tissue. The only nephroma which we encounter is the so-called Wilms' tumor. This tumor contains all the histological elements of the kidney and is truly nephroid. To use terms such as "histoid," "organoid" and "hypernephroid mesothelial type of hypernephroma" confuses the issue and conveys nothing concrete. To disbar the use of "oids" in the classification of neoplasms in and on the kidney would greatly simplify our understanding of them and pave the way for a clearer conception of their behavior and their response to therapy.

Hypernephroma.—The hypernephroma is not a true kidney tumor but is derived from congenitally misplaced suprarenal tissue. Such misplaced tissue has been found widely distributed within the abdomen and even along the spermatic cord in the inguinal canal. Wide distribution can also take place anywhere on or within the renal organ. The reports of Martland and O'Crowley on autopsies in accidental deaths give conclusive evidence in support of this possibility. The deposit of embryonic rests makes possible the development of a hypernephroma on, underneath or anywhere in the renal parenchyma, and to say that a hypernephroma develops only on the capsule of the kidney is untrue. It is the only neoplasm reportedly found associated with polycystic kidney disease and is the most common renal neoplasm in the pregnant woman, which suggests an hormonal factor as the activating agent. These tumors are most common in the 6th decade of life and are rarely reported in children. Other than Wilms' tumor, they are most frequently discovered accidentally by the physician. The early stage of their development is relatively slow, they are encapsulated and sometimes grow to large size or become large by intratumoral hemorrhage. At other times the primary tumor is secondary in size to the metastatic lesion, and such a condition complicates the clinician's responsibility respective to a correct diagnosis.

Nephroma (Wilms').—The 53 names applied to this tumor which is commonly found in children would be almost a day's assignment for a medical student to memorize. The Wilms' tumor may be a true embryoma, but it seems logical that since it is the only renal tumor which contains all the elements of the kidney it has justly earned the distinction of being called a nephroma after its name has been bandied about for 123 years. It will require some effort to make this term universal, but it is wise to make the effort in order to clarify the terminology. It is one of the largest renal neoplasms in children, grows rapidly and metastasizes relatively early either by direct invasion or blood stream. In children it makes no selection of side or sex; in the adult, it is rare but does occur in every decade up to and including the eighth with a high preference for the male sex. Many of these tumors are accidentally discovered on routine examination in children's clinics and hospitals. Ladd of Boston has had one of the largest experiences with children's renal tumors and reports 60 to 70 per cent of renal tumors to be of this type. In our clinic of general urology only about 30 per cent of renal tumors in children belong to this class, the others being carcinoma, both embryonic and adult, and neuroblastomas and sympathicoblastomas. Several writers have reported bilateral involvement with nephroma. The fact that these tumors have been found in foetuses, have been removed surgically within the first three days of life and that 75 per cent are found before the fifth year leaves no doubt that they belong to the embryonic group of neoplasms. Because of the rapidity of their growth, their high degree of malignancy, and the great uncertainty as to the results of surgical treatment they still present a challenge to Medicine.

Neurogenic tumors of the kidney.—Tumors derived from the neurogenic anlage include the neuroblastoma, sympathicoblastoma, medulloblastoma, ganglioneuroma, paraganglioma and schwannoma, and take their origin from the nerve structures about the kidney and adrenal gland. They used to be called sarcomas. Such tumors are found close to the kidney pelvis, anterior, posterior or below it. They cause an obstruction to the ureter and interfere with the pyelographic pattern to the extent that it is impossible to predict their origin preoperatively. The most embryonic, the neuroblastomas and medulloblastomas, grow rapidly. There can be but little significance in the so-called Pepper and Hutchison types. The difference is not in the histology of the tumor but in the mode of its dissemination. The avenues for metastatic development can be explained by Anson's work on the difference between the venous drainage of the right kidney and of the left kidney. The right perirenal lymphatic drainage is in close approximation to the liver, which accounts for the metastases to the liver; while the dissemination from a left kidney tumor is directly through the renal vein to the prevertebral system and upper skeletal region. We are indebted to Pepper and Hutchison for their differentiation of behavior with respect to the development of metastases but to Anson for a possible explanation of the biological behavior of the left renal tumor. The ganglioneuroma and paraganglioma are more adult forms of nerve tumors. The latter are chromaffin tumors and grossly are reddish in color, show a lesser degree of malignancy and do not possess any sex hormone. The schwannoma is rare, as only six or seven tumors are reported. These develop below the kidney but their x-ray shadows often overlie the kidney shadow, and they are difficult to diagnose clinically. However, they can usually be removed without disturbing the kidney and ureter and are not possessive of a high degree of malignancy. The clinician can conceive of these tumors of neuroectodermal origin as perirenal tumors possessing the behavior characteristics of the same types of tumors found in the brain and spinal cord.

Sarcomas.—The difference between sarcomas and neurogenic tumors is now well recognized, and tissue strains have done much to segregate these tumors into proper categories. However, sarcoma of the kidney does occur arising from structures at the hilum adjacent to the pelvis, from the capsule or even from the kidney itself. Such growths become fairly large and are more apt to invade the kidney than the neurogenic tumors. They occur in all age groups but are not common. They often appear fairly well encapsulated at first and may be associated with renal calculi. The roentgenograms of sarcoma may show spotty areas indicating fatty tissue which often suggests their type. They usually grow rapidly and are locally invasive of the kidney and perirenal tissues. They can be removed without much difficulty unless they are invasive of the posterior abdominal wall, and they are not usually considered as malignant as the other tumors.

Carcinoma.—The carcinomas of the kidney cortex are seen at all ages and may be divided into the embryonic and adult types. The embryonic tumor takes its origin in the renal blastema while the adult carcinoma may arise, according to Cabot, from an adenoma, which is not an uncommon finding in the kidney, or from any of the tubules. The adult types frequently present an adenomatous character and are apt to develop into large lobulated masses. The embryonic cancer grows rapidly, infiltrates the whole organ and metastasizes to the lungs through the blood stream. The embryonic tumor is more often found in the child or young adult. The adult type grows slowly, at first is encapsulated and may be accidentally found on routine physical examination before it has penetrated the pelvis and caused hematuria. It infiltrates the renal organ and may infiltrate the liver or spleen. The behavior of these tumors is much like the behavior of adenocarcinomas elsewhere in the body. The embryonic type is the more malignant of the two.

Papillary carcinoma.—Papillary cancers of the kidney pelvis are similar to transitional cell papillomas of the urinary bladder. While it has been known for many years that papillomas of the kidney pelvis metastasize to the ureter and bladder it is only within the past few years that reports have been made concerning such metastatic lesions from papillary carcinomas of the renal cortex. We have made a study of cortical cancers which have showed a papillary character. They may include the papillary adenocancers. All cancers with papillary cellular structure, whether derived from the kidney cortex or pelvis, behave similarly. They are not encapsulated, they bleed readily, infiltrate the kidney, and metastasize not infrequently to the lower ureter and to the lung. One has a right to ask whether all of these papillary tumors do not take their origin from the pelvis, some of whose embryonic cells have reached well within the component parts of the renal blastema. Twenty years ago we removed a cancer of the kidney and seven years later the patient had a tumor of the lower ureter. This was removed. Two years later he had bloody sputum and a radiogram positive for metastatic tumor in the chest. In review of the microscopic sections the primary tumor was found to be of papillary character. Three years ago the right kidney of a physician 42 years of age was removed by a general surgeon for malignancy. Two years later the lower end of the ureter was removed because of bleeding. One year later the patient was referred to us for hematuria and dysuria. He was found to have an infiltrating tumor of the base of the bladder with no other evidence of cancer. Biopsy indicated the same microscopic picture of papillary carcinoma in all the specimens. The origin of the primary tumor was cortical rather than pelvic. A ureterosigmoidostomy was done on the remaining side and his whole bladder removed. He subsequently developed a metastatic lesion in his abdominal wall and died of the disease. Time forbids a discussion of the theories of transmission of papillary renal tumors to the lower ureter and bladder, but other reporters have made observations like ours and we are in accord in advising complete ureterectomy including a portion of the bladder for all tumors of the kidney, whether cortical or pelvic, which present a papillomatous character. The other tumors of the kidney pelvis, such as the scirrhus and epidermoid types, belong to the same category as the papillary carcinomas, show the same biological behavior as the papillary carcinomas and demand the same serious consideration for treatment. A difference in degree of malignancy of a tumor of the kidney pelvis has little significance when all have such a high degree of potential growth and are ultimately fatal.

Metastatic developments.—Neoplasms of the kidney present as many, if not more, problems dealing with metastases than any other group of neoplasms. The surgeon many times removes renal neoplasms when the prognosis seems good only to find that some time within one year to twenty years the patient has a metastasis. Beer wrote many years ago, "we do not know what biological forces delay the development of secondary tumors." All the reports containing the largest series of cases are in accord that renal tumors metastasize to the lungs, bones, liver, regional lymph nodes, spleen, adrenal, opposite kidney, heart, brain and seminal vesicles in that order of frequency. (Abeshouse and Wienberg; McDonald and Priestley; Smith, Deming.) Thus to recommend the resection of the para-aortic lymph glands, whether they are involved or not, in all cases of renal neoplasms does not appear sound. The hypernephroma, the nephroma (Wilms'), embryonic cancer, and the papillomas may by-pass the local lymph nodes and present their secondary growths in the lungs and bones; while adult cancers, together with the adenocarcinomas, the scirrhus cancers and sarcomas, do involve the local regional lymph glands at the hilum of the kidneys and may be considered for resection at the time of the nephrectomy. If one keeps in mind the behavior of the different types of renal tumors and follows each patient after nephrectomy to his death the real facts appear: that a good number survive five years but die of a metastatic lesion or lesions between the 5th and 10th years and some even later. Graves reports the case of a patient who died of metastasis 20 years after the original tumor was removed, and there are a number of patients in our series who died of the disease between the 10th and 15th years. So far, we do not know what forces check the growth of these tumors for many years. To go one step further, Bumpus, Beer, Hyman and Mann have reported the spontaneous disappearance of lung metastases. Churchill and Barney report the successful removal of a solitary nodule in one lung, and a long follow-up period indicated that the patient remained in good health without further evidence of the disease. The existence of a solitary metastasis must be an exceedingly rare condition, but these cases of spontaneous disappearance of the secondary lesions relate entirely to the hypernephromas and not to the other types of renal tumors.

Radiation of renal neoplasms.—Radiation of renal neoplasms has been applied in a desultory manner. Waves of enthusiasm have been followed by waves of defeatism, and it would seem that no one has really crystallized this form of treatment for clinicians. Radiation has been used as the last straw or because it was thought that it might play some part in preventing metastases. The only sound basis for radiation is the sensitivity of the tumor. It is known that the nephroma (Wilms'), the hypernephroma, embryonic carcinoma and the sarcoma respond to radiation. Wharton suggests radiation of nephroma (Wilms'), while Ladd deprecates its value; Munger believes that radiation does only temporary damage to neoplasms. To radiate large kidney neoplasms or deep-seated metastases with the hope of full control is folly. Radiation will reduce the size of the responsive tumors but as far as complete control of the growth is concerned we can not yet expect full control of the tumor growth by radiation alone. One can expect cessation of bleeding, and we have used x-ray therapy in conjunction with ligation of the ureter to stop bleeding and for palliation in patients who have an inoperable tumor. However, proof that roentgen therapy will control the growth of renal tumors has not yet been given. Certainly, it should not be employed until a microscopic study has been made to determine the tumor's type and hence its probable sensitivity to radiation.

Treatment of renal neoplasms.—Nephrectomy has always been and still is the treatment for malignant disease of the kidney provided the growth can be removed. Much interest has been shown with regard to the operative approach to the tumor. The loin incision has for many years maintained its popularity, but during the last 3 years Chute and others have favored the transthoracic approach as giving an unexcelled exposure of the tumor and the pedicle of the kidney. No doubt thoracic surgery has influenced and stimulated this method of approach, and numerous operators in various countries have successfully performed nephrectomies by this route. More recently, Nagamatsu has suggested a dorsolumbar approach with subperiosteal resection of segments of the tenth, eleventh and twelfth ribs to avoid traversing the thoracic cavity. Both incisions have been used in our clinic and have given equal satisfaction in exposure of the pedicle. Ladd advises the transabdominal approach and ligation of the vessels before mobilizing the tumor and shows statistically superior results. This is possible in children but more difficult in adults. There is no doubt that much is to be said in favor of ligating the pedicle before freeing the kidney and tumor for in so doing the many tumor cells which might be scattered through the blood and lymph streams are held in check. When the tumor is inoperable a biopsy should be taken and the ureter ligated, provided the kidney is not infected; and supplemental x-ray therapy may be given if the tumor is radiosensitive. It would seem unnecessary to resect the peri-aortic lymph glands in those tumors whose metastases ordinarily occur through the venous blood stream to the lungs and bones. Surely patients with papillary tumors of the renal cortex and all patients with tumors of the pelvis should routinely have a removal of the ureter and segment of the bladder. We believe that the surgical technique concerning renal tumors is now clearly defined but we urge that the surgeon at the time of nephrectomy ascertain by immediate biopsy the type of tumor with which he is dealing.

Results.—The control of renal neoplasms, except for the nephroma and neurogenic tumors, can not be determined by a 5-year follow-up or even by a 10-year follow-up. We have in our clinic records of 132 consecutive renal tumors in the past 25 years. All have a microscopic section. All have a complete follow-up to date or to the death of the patient. The control of the renal tumors in the above series by nephrectomy is 9.0 per cent. This is humiliating, but if one compares these results with the results of treatment of malignancies of other internal organs it is not too bad when compared with lung cancer at 2 per cent, gastric cancer at 6 per cent and prostatic cancer at 5 per cent.

The author feels that our past conception of control of renal malignancies has been incorrect and that we have been far too optimistic regarding the actual results. The only true determination is the complete follow-up of every case. In every case, a microscopic study of the tumor should be made and its character noted. The reports by Foot, Humphreys and Whitmore of 295 cases are instructive but there are too many indeterminate cases, although they have made allowances for the cases which have not been followed to the end. Ladd presents a remarkable report on the treatment of children's renal tumors. Priestley and Broders add another favorable list. The many individual reports of a few successful controls add interest but do not help us arrive at an absolute conclusion. The author does not place much credence in the difference between a granular cell or clear cell hypernephroma because both tumors prove to be lethal if left in place. Tumors do vary in degree of malignancy and patients vary in their defense to malignant growth, but the surgeon should not take credit for the control of a renal malignancy which he has removed until the patient has survived 15 to 20 years without a recurrence or autopsy reveals no evidence of tumor.

We have taken the challenge of the problem of renal tumors seriously and attempted to disclose why we can not obtain better results. We have noted the delay in diagnosis and treatment as applied to the doctor and patient, the doctor alone and the patient alone. We would like to lay some of the blame upon the procrastination element, but we can not do it. Patients who refused early treatment and patients whose doctors prescribed styptics and pink pills to stop bleeding have the same recovery record as the 45 per cent whose tumors gave no symptoms, were accidentally found and were immediately treated. The biologist might truly argue that the delayed cases had time to develop a defense mechanism to the tumor growth. The typing of these tumors has not been of any particular advantage in solving this problem of control. Is the tumor malignant or is it not? Will it metastasize by lymphatic channels or by way of the blood stream? Is it radio-sensitive? We have no way to measure a patient's resistance to tumor growth. We have advanced in our knowledge of the behavior of renal tumors and have developed a sound surgical approach to their removal, but even with the

Papanicolaou stain of the urines, new serological tests for cancer and cystoscopy and x-ray procedures by means of which an early diagnosis can be made, the enigmas of the problem seem almost insurmountable and the challenge to raise the actual percentage of control of renal tumors and their metastatic lesions is as great as ever. This challenge the author begs the urologist to accept and to make another effort to improve the percentage of control by the use of radioactive isotopes in association with surgery. The research of Moore and his coworkers in Minneapolis, Davis in Chicago and Selverstone and White in Boston indicates not only a high degree of accuracy in determining the presence of nerve and epithelial tumors and sarcomas with radioactive isotopes but a precise focal localization in 95 per cent. Malignant tumors of the kidney contain these tissue elements. The isotope diiodofluorescein has a special affinity for tumor cells so that not only the primary tumor but the metastatic transplants to lymph nodes and peritoneum are readily detected. The technical procedure is not difficult in its application and would add but a few minutes additional time for the operating surgeon with the assurance of localizing tumor tissue and recognizing the lymph glands involved in metastatic renal tumor so that such tissues which might otherwise be left behind can be removed if operable. Sufficient work with tumors using radioactive isotopes has already been done to conclude that their use in conjunction with the surgical treatment of renal tumors is well within the realm of our present-day consideration. We are living in the atomic age. We must be atomic urologists and invoke the use of the radioactive isotope, for it is reasonable to expect that it will provide the next cog in the chain of our efforts to control renal malignancies.

SUMMARY

A plea is made for a simple classification of renal tumors based on their tissue origins and biological behavior.

The exposure of large renal tumors by the transthoracic route or Nagamatsu incision offers technical advantages in the adult patient.

Biopsy of every renal tumor should be made at operation.

Lymph node resection of para-aortic nodes is necessary only in those tumors which biologically metastasize to local lymph nodes rather than through the blood stream to distant organs.

The enigmas of renal tumors will persist until the cause of renal malignancy is divulged.

The challenge for an improved percentage of control of renal malignancy may reasonably be found in the use of radioactive isotopes.

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CARCINOMA IN A POLYCYSTIC KIDNEY

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The combination of a malignancy and polycystic disease in the kidney is a rare combination. In 1934, Walters and Braasch reported 3 cases of malignancy occurring in a polycystic kidney. Only one of these cases, an adenocarcinoma, grade 3, was reported in any detail. In 1937, Tomaff reported a case of "Hypernephroma With Polycystic Degeneration" but no mention was made of any pathological findings. Melicow and Gile reviewed the literature in 1940, and added a case of their own. Theirs was the first detailed report of a hypernephroma in a polycystic kidney, and the only case in which the diagnosis was made preoperatively. A similar case was reported in detail by Bobbitt in 1943. The latest report of this rarity was in 1946 by Hayward. Hayward's case, a hypernephroma, was similar to ours in that polycystic disease was not suspected preoperatively and no pathological changes were noted in the opposite kidney. The cases of Melicow and Gile, Bobbitt and Hayward are the only full case reports in the literature. The pathology in these 3 cases was identical. Two cases, an angiomyosarcoma and a fibrosarcoma occurring in polycystic kidneys, were reported by Lowsley and Curtis in 1945. This brings the total number of cases in the literature up to eight. All have pathological confirmation. A benign intracystic papilloma in a polycystic kidney was described by Wells in 1936. Our case but for its malignant changes is similar to Wells' case.

It was our privilege to observe a case of malignant papillary cystadenomas in a polycystic kidney. This case is reported because of its rarity and interesting aspects.

CASE REPORT

A 58-year-old laborer entered the Veterans Administration Hospital, Lincoln, Nebraska on February 5, 1948, with complaints relative to his lower extremities suggestive of occlusive peripheral vascular disease, due to arteriosclerosis. No genito-urinary symptoms were present.

Physical examination revealed a well-developed, slender, white male of the stated age, not acutely ill. Heart and lungs were negative. Blood pressure was 160/95; pulse was 92, regular and of good quality. Abdominal examination was essentially negative. Myocyanosis of both feet was present.

Bilateral dorsalis pedis pulsation was easily felt. There was a slight coldness of both feet. The initial impression was obstructive peripheral vascular disease, due to generalized arteriosclerosis.

Because of the slightly elevated blood pressure, an excretory urogram was obtained and revealed distortion of the calyces in the left kidney, with outward displacement. A tentative diagnosis was made of a possible tumor or solitary cyst of the left kidney. Bilateral retrograde pyelograms made with diodrast re-

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vealed a definite distortion of the superior calyx on the left in the form of a sweeping curve which suggested a solitary cyst or renal tumor. The right retrograde pyelogram was considered normal. X-ray of the chest was negative. X-ray of the extremities for evidence of calcified vessels was negative.

Urine examinations on several occasions were normal. Blood chemistry studies were within normal limits. The Kahn test was negative.

A paravertebral block was performed on the left side, and was followed by improvement in circulation, so that a left lumbar sympathectomy was recommended by the general surgical service.

On March 16, 1948 left lumbar sympathectomy and left nephrectomy were performed. Exposure of the left kidney revealed a slightly enlarged polycystic kidney, with a small oval, firm nodule at the lower pole. A biopsy from the nodule was reported as malignant. A left nephrectomy was done.

Postoperatively the patient responded well. He was ambulant on the third postoperative day and the sutures were removed on the eighth day. The wound was well healed. The patient responded well to left lumbar sympathectomy, noting relief from pain, cyanosis, and sweating.

Pathological report (Dr. Paul Kisner): Specimen consisted of a left kidney which weighed 185 gm. and measured 12 cm. in length, 6.5 cm. wide in the midportion and 3.8 cm. thick in the midportion. The external surface showed numerous thick-walled cysts, varying in size from 2 mm. up to 1.8 cm. in diameter. These cysts were uniformly distributed throughout all portions of the kidney. The kidney surface was smooth and glistening with the exception of the cysts. Upon puncturing the cysts adjacent to the surface, a thin brown-colored fluid could be expressed. Section of the kidney disclosed numerous, large cysts in the medullary portion which varied in size from 3 mm. up to 2.1 cm. in diameter. In the lower pole four small tumor nodules varying in size from 2 mm. up to 7 mm. in diameter were seen. These tumor nodules were yellowish gray in color and moderately firm in consistency. The pelvis was moderately compressed due to large cysts. The mucosa of the pelvis was slightly hemorrhagic, but otherwise showed nothing of importance.

Numerous sections taken for microscopic examination revealed several sections of the tissue showing numerous, small cysts, filled for the most part with a thin, light pink-staining material. A few of these cysts appeared to be dilated tubules which were filled with a thick, dark pink-staining colloidal material. A biopsy specimen taken for frozen section and then for paraffin section was composed entirely of tumor tissue which was anastomosing papillary structures, lined by a single layer of columnar epithelium.

The striking feature was the presence of small collections of lipoid containing foam cells, which were a part of stromal reaction and not neoplastic. There was no evidence of capsular formation and the neoplastic invasion into the parenchyma appeared to be uninhibited. There was only mild malignant mytosis. A diagnosis was made of polycystic renal disease, with papillary cystic adenomas, malignant, grade 1. Follow-up examinations, 3 months, 6 months and 2 years postoperatively revealed no evidence of metastasis or renal failure. Postoperative excretory urography performed during the follow-up examinations have revealed no change in the right pyelogram.

SUMMARY

A review of the literature of a renal neoplasm occurring in a polycystic kidney has been presented.

A case of malignant papillary cystadenoma in a polycystic kidney is reviewed, the ninth to be reported in the literature.

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SPONTANEOUS BILATERAL PERIRENAL HEMATOMA

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Although hematomas about the kidneys are seen not infrequently, those hematomas which are of spontaneous, nontraumatic origin are relatively rare, and rather infrequent reports concerning them are to be found in the literature. In 1933, Polkey and Vynalek made a thorough review of all the literature concerning spontaneous perirenal hematomas reported up to that time, and found a total of only 178 such cases. Since that time the additional cases that have been reported in the American literature are by: Aschner and Klinger, Miller and Cordonnier, Fort, Scrivner, Longmire, Irwin, Keefer, Coppridge, Moore, Counseller and Emmett, and Wever and Perry.

In their series Polkey and Vynalek found that the causative factors responsible for the perirenal hematomas were most commonly renal diseases such as nephritis, renal tumors, infections, etc., and that these comprised 69 per cent of the cases. Disease of the blood vessels accounted for 29.2 per cent of these cases, the most common being arteriosclerosis, and peri-arteritis nodosa, which accounted for 7 cases of the 178.

The symptomology and diagnosis of this condition have been discussed in sufficient detail in previous articles as to require little additional comment except to note that the condition has been correctly diagnosed in only a relatively few cases, the differentiation with perinephric abscess, tumor, or acute intra-abdominal conditions being often very difficult. However, the diagnosis of perirenal hematoma may be made if a patient suddenly has an attack of pain in the region of the kidney which is followed by the signs of internal hemorrhage and a mass in the flank.

In regard to treatment, it is of interest to note in Polkey and Vynalek's report that of 47 cases where treatment was conservative and expectant, the mortality was 100 per cent. When conservative surgical procedures such as evacuation of blood clots and drainage were used, as was done in 43 cases, the mortality was reduced to 40 per cent. When nephrectomy was used, as in 62 of the cases, the mortality was reduced to 24 per cent. At present nephrectomy still appears in general to give the best results, although occasional cases such as the case of Aschner and Klinger in 1951 have been treated successfully with more conservative measures.

Reports of bilateral spontaneous perirenal hematomas are very infrequent in the literature, and of the 178 foregoing cases, only five were bilateral. Two of the bilateral perirenal hematomas were caused by nephritis, one by aneurysm of the renal artery, one by adrenal hemorrhage, and one by peri-arteritis nodosa, as was the case being here presented. The following is a report of a case of bilateral spontaneous perirenal hematoma caused by peri-arteritis nodosa:

CASE REPORT

A 36-year old white man was admitted to the hospital April 18, 1950, with gross hematuria, burning on urination, frequency of urination, and nocturia.

The symptoms began about 1 week prior to admission, following an upper respiratory infection. Since the onset of symptoms the patient had been aware of swelling of his eyelids. He denied any previous illness except psychosis treated with shock therapy in 1944. On admission his blood pressure was 170/105, temperature 98.5F, pulse 76, respirations 20. He had edema of both lower eyelids. The chest was clear, the heart was not enlarged to percussion and no murmurs were heard. The abdomen revealed no tenderness or abnormal masses, and the liver, kidneys, and spleen were not palpable. The clinical impression was that of acute nephritis. Laboratory findings: Red blood cells 5,060,000, hemoglobin 14 gm., white blood cells 10,200, nonprotein nitrogen 33.3 mg. per cent, creatinine 1.1 mg. per cent, cholesterol 166.6 mg. per cent. Urinalysis revealed specific gravity 1.012, trace of albumin, no sugar, and numerous red blood cells. Retrograde pyelogram was negative. Throughout the hospital stay the patient's temperature ranged from 99.6 to 101F. Prothrombin time 87 per cent of average normal, prothrombin concentration 63 per cent. Serology negative. Smear and culture of bladder urine were negative for tuberculosis. Urine culture showed a growth of beta hemolytic streptococcus. Platelet count was 376,800. Five additional examinations of the urine showed very faint trace of albumin. The urine cell count decreased to 1 red blood cell and 1 white blood cell. The patient improved throughout the hospital stay and was discharged on April 28, 1950 with no hematuria but his temperature still stayed around 100F.

The patient was re-admitted 3 days later. He now complained of onset of pain in the right flank suddenly after having a bowel movement, the day before admission. The pain was sharp in character and radiated from the back and flank along the crest of the ileum but not down into the leg or scrotum. With the onset of pain the patient was unable to urinate, except for a very small amount the night before admission and on the day of admission. The patient denied hematuria. Physical examination revealed the patient to be in no acute distress. Blood pressure was 140/76. The patient was experiencing right flank pain on deep respiration. Examination of the abdomen revealed that the bladder was distended one-half the distance between the pubis and the umbilicus. Moderate tenderness was present about the left groin and flank. The liver and spleen were not palpable. On rectal examination, there was no tenderness. The prostate gland was firm and nontender. It was not enlarged. On admission an indwelling catheter was inserted and 350 cc. urine obtained. Blood count showed a red blood count of 2,780,000, 8 gm. hemoglobin, 51.2 per cent. White count 8,600. Nonprotein nitrogen was 42.5 mg. per cent. Urinalysis showed specific gravity: 1.016, plus 1 albumin, negative sugar, 2 white cells per high power field. Excretory and retrograde urograms showed displacement of the right kidney and apparent obliteration of the right psoas shadow, strongly indicating the diagnosis of perinephric abscess. Until May 6 the patient's temperature varied from 101 to 103.6F. The nonprotein nitrogen was 40 mg. per cent. Two additional blood counts showed a rise in the white blood cells to 12,750 and then 24,900; urine cultures showed paracolon bacilli. The patient was taken to the operating room, and the right perirenal space was found to contain firmly adherent dark brown blood clots. The kidney was normal in consistency and there appeared to be no tumors within the kidney. On the anterior surface of the kidney there were two small grayish spots resembling infarcts. A portion of the clots was removed, but the greater portion appeared to extend medial to the kidney toward the large vessels and peritoneum, and since no active bleeding was present these clots were not disturbed. A drain was inserted and the wound was closed. The patient's temperature gradually subsided. The nonprotein nitrogen dropped to 26.1. The blood culture was negative after 10 days. The urinalysis continued to show very faint traces of albumin and also faint traces of sugar and the cell count was normal. On May 10 the patient had a convulsive seizure at which time the blood pressure was 170/114. Following the seizure the patient responded well to questioning. The following day the patient had some vomiting, headache, blurred vision, dizzy spells and periods of nervousness. It was noted that the patient was having definite periods of confusion. On May 16 the patient was improved and was discharged, transferred to the State Hospital because of psychosis.

The patient was readmitted July 3. Several days previously the patient had chills, fever, pain in the left flank and left lower quadrant, accompanied by profuse diaphoresis. He had no urgency, but there was frequency and nocturia. The patient denied hematuria. Physical examination revealed the patient to be profusely sweating. The blood pressure was 180/100. The temperature was 100F, pulse 100, respirations 34. The examination of the heart revealed a short, sharp, systolic, mitral murmur. Examination of the abdomen revealed a right healed, lumbar scar intact except for a small sinus. The left kidney was found to be palpable and tender. During the first 15 days of hospital stay the patient ran a low grade fever, occasionally as high as 101.4F. Examination of the urine revealed essentially negative urinalysis except for 7 red blood cells per high power limits, and urine cultures were negative. Two examinations of the feces for occult blood were positive. X-ray studies revealed lobular atelectasis of the lower lobe of the left lung on July 3, negative retrograde pyelogram except for malrotation of right kidney and slight mesial displacement on July 6. X-ray examination of the gallbladder, upper gastro-intestinal tract, colon and skull were negative. On July 20 the patient was taken to the operating room and a transabdominal left nephrectomy was performed. The patient did fairly well, the postoperative elevation of temperature subsiding in 5 days. The nonprotein nitrogen went as high as 86 mg. per cent and then subsided to 46.1 mg. per cent. Bone marrow smear done on July 20 showed that the marrow contained a large number of atypical cells with many polymorphonuclears having nuclei with 8 to 10 segments. The eosinophiles were in the upper limits of normal. The proportions of red and white blood cells were about 1 to 12 (normal about 1–4). This indicates rather severe bone marrow injury with abnormal young and adult forms. The evaluation of the coagulation mechanism of the body on August 2 revealed: 1) clotting time normal; 2) no evidence for circulating anticoagulant; 3) no increased activity of fibrinolysin; 4) normal clot retraction; 5) normal prothrombin time; 6) normal bleeding time; 7) questionably positive Rumple-Leid test (65 per cent drop); 8) eosinophilia from 750 to 1000 per cubic millimeter; 9) border line low platelet count. This indicated approximately normal coagulation mechanism and vessel wall reactivity. The patient was discharged on August 5 in fairly good condition.

Study of the specimen showed that the left kidney and capsule weighed 963 gm. The kidney was greatly enlarged and its surface was light red with numerous irregular, dark red pitted scars. The capsule in some areas measured 2 cm. in thickness and consisted of firm fibrofatty tissue with areas of hemorrhage and necrosis. When the capsule was stripped, the kidney was found to be partially surrounded, and separated from the capsule by very extensive subcapsular hemorrhage.

Microscopic examination showed extensive subcapsular hemorrhages of the left kidney with thrombosis of the veins within the kidney. In these sections there was no evidence of primary disease of the blood vessels, except for evidence of arterial hypertension.

The patient was readmitted November 27. The patient had done very well since discharge until 1 week before this admission, when he noted loss of appetite followed by nausea, and a decrease in total urinary output. He also had dryness of the throat and for the past 3 days headache, vertigo and dyspnea with nonproductive cough. Examination revealed the patient to be acutely ill. The blood pressure was 210/130, temperature 96F, pulse 100, respirations 40. The lips were pale and tongue was coated and furred. The patient was markedly dyspneic, with shallow, labored respirations. The lungs were clear. The abdomen contained a questionable epigastric mass which felt smooth and tender, and was slightly tympanitic. There was tenderness in the right lumbar fossa. Urinalysis: specific gravity, quantity not sufficient. Albumin 4 plus, sugar negative, white blood cells 150–200, red blood cells 0–1. Blood count: red blood cells 2,060,000, white blood cells 12,450, hemoglobin 6.5 gm. or 41.7 per cent. Nonprotein nitrogen 150 mg. per cent. The temperature spiked from about 96.6 to 102F, the pulse remaining constantly elevated and the respirations varying between 20 and 30. The patient remained constantly very pale and dyspneic. The respirations remained labored throughout the hospital stay in spite of an oxygen tent. The tenderness in the upper abdomen persisted and oliguria became even more pronounced in the following days so that only a few drops of urine could be obtained per day. On the third hospital day he became semicomatose and started vomiting frequently. A repeat urinalysis revealed essentially the same findings as the first day of admission. He received two blood transfusions, but had no noticeable improvement. The patient died December 1, 1950.

Autopsy disclosed peri-arteritis nodosa with characteristic vascular lesions in the coronary, pancreatic, renal, adrenal and prostatic arteries and generalized lymphadenopathy; uremia with uremic arteriolar and glomerular changes in the right kidney; marked cardiac hypertrophy and dilatation with congestion of the spleen, liver, gastro-intestinal tract, ascites (1000 cc), bilateral hydrothorax (rt. 1500 cc, lt. 500 cc); organizing pneumonia of both lungs, left surgical nephrectomy and nephrectomy scar; right flank surgical scar and perirenal fibrosis; chronic cholecystitis; congestion and edema of the bladder (indwelling catheter).

Peri-arteritis nodosa itself was first described by Kussmaul and Maier in 1866; when an exhaustive review of the world literature was made by Boyd in 1939, only a total of 395 cases had been reported. However, since that time, cases have been reported with rapidly increasing frequency.

It is of great interest to note that in recent years many have come to believe that peri-arteritis nodosa is the result of an allergic vascular reaction. Rich, in 1942, showed that the disease often appears following serum sickness or sensitivity to sulfonamid compounds. Allen, in his book *The Kidney*, published in 1951, states: "The pathogenetic role of hypersensitivity developed during the course of a prolonged infection was stressed by Gruber, convincingly reaffirmed by Spiegel, and subsequently effectively investigated by Rich with particular emphasis on the effects of the sulfonamides. The hypersensitive concept of the nature of peri-arteritis nodosa is now generally accepted. Supporting evidence for the allergic hypothesis from human material is derived from the eosinophilia in the peripheral blood and in the local lesions, the fibrinoid alteration in the vessels, and the common association with asthma and glomerulonephritis. Because of the increased opportunity for sensitization on account of the use of antibiotics, vaccines, and sera in wholesale quantities, it is believed that the incidence of peri-arteritis nodosa has increased considerably in recent years." The importance of these factors in relation to spontaneous perirenal hematomas becomes apparent from the fact that the most commonly involved organ of the body in cases of peri-arteritis nodosa is the kidney. Arkin showed that at necropsy 80 per cent of cases of peri-arteritis nodosa showed renal involvement. Ralston and Kvale in 1949 in a study of 30 cases found that renal insufficiency was the immediate cause of death in a third of the cases. In one of these there had been a large perirenal hemorrhage from a hemorrhagic infarct in one kidney. Therefore, with the increasing incidence of peri-arteritis nodosa as noted by Allen, and the high percentage of pathological renal involvement present in this disease, one is led to expect that peri-arteritis nodosa will become increasingly more prominent as an etiological factor causing spontaneous perirenal hematoma.

SUMMARY

A case of spontaneous perirenal hematoma is presented, with perirenal hemorrhage occurring about one kidney and treated with conservation of the kidney by evacuation of blood clots and drainage. Subsequently a second subcapsular spontaneous perirenal hematoma occurred about the second kidney, requiring nephrectomy. The causative factor of both of these hematomas was found to be peri-arteritis nodosa. The literature is briefly reviewed and the increasing incidence of peri-arteritis nodosa noted.

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CYTO-DYNAMIC PROPERTIES OF URINARY NEOPLASMS: III. CULTIVATION IN VITRO OF CARCINOMA OF THE KIDNEY

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In previous reports the cultivation in vitro of transitional cell carcinoma of the ureter[1] and maintenance of "hypernephroma"[2] have been reported. The opportunity to view growing carcinoma of the kidney has been intriguing since there are many curious histological observations about the neoplasm itself. Within a single specimen the morphology varies greatly and the exact meaning of these variations has not been understood. (Caspersson A & B cells?) The question of origin of the neoplasm has not been thoroughly established, whether one portion of the nephron contributes to the original prototype or whether different portions of the renal unit can give rise to different types of renal neoplasm or to the variations within a simple neoplasm. The detection of hypernephroma cells in urinary sediments has been difficult. The opportunity to test various anticarcinogenic agents against this type of tumor has been presented by cultivation in vitro.

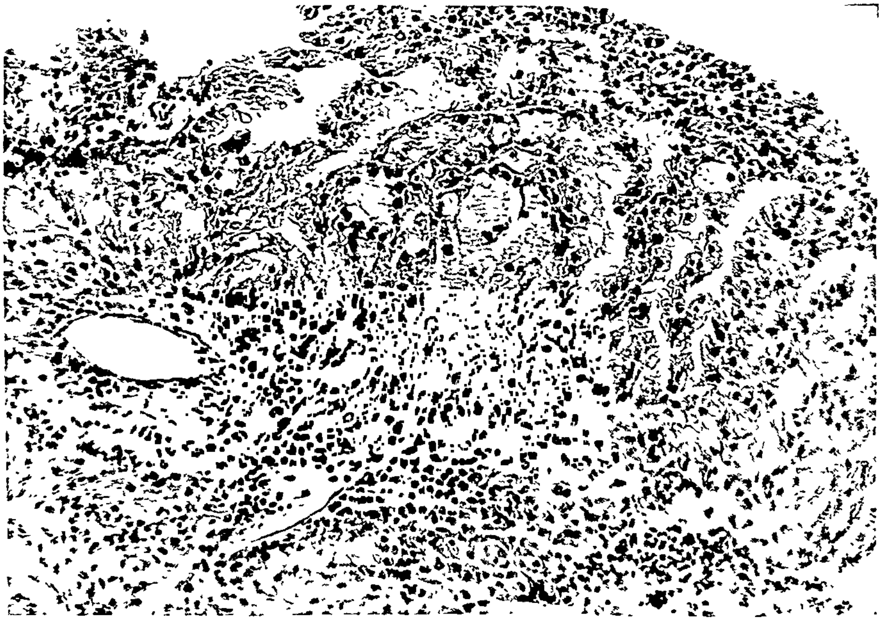
FIG. 1. Original explant, carcinoma of kidney, growth pattern resembles that of cultures (H & E stain).

METHODS

Tissue was obtained aseptically from a fresh surgical specimen, histology of which is presented in figure 1. The tissue was cut up into small fragments approximately 1 mm. square, washed several times with Simm's solution to which 100 units of penicillin per ml. and 5 mg. of streptomycin had been added. The fragments were then transplanted into square roller tubes whose interior surfaces had

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[1] Bunge, R. G. and Stein, R. J.: J. Urol., 64: 646, 1950.
[2] Stein, R. J. and Bunge, R. G.: J. Urol., 66: 103, 1951.

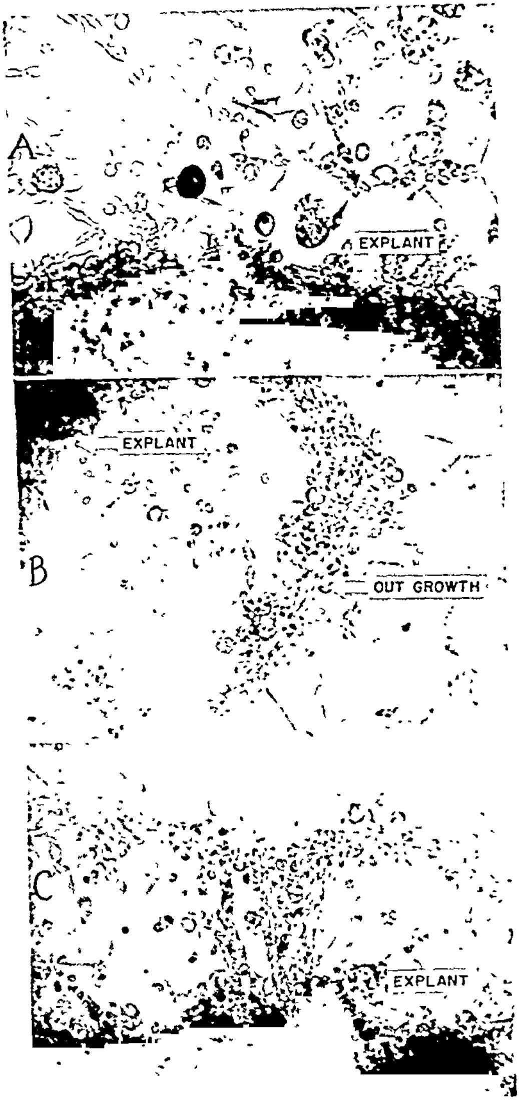

FIG. 2. *A*, 7-day culture in White's medium. Some fibrocytic proliferation and epithelial "sprouts." No active growth of epithelium. *B*, 8-day culture in equal parts of autologous serum and White's medium. Epithelial outgrowth tending to form bridge. *C*, other growths projecting outward and then proliferating parallel to explant.

been prepared in advance with a thin layer of rooster plasma. Media employed were equal parts of autologous serum and White's synthetic medium and White's medium alone.[3] Tubes were placed in a roller drum and incubated at a temperature of 37°C. The medium was changed whenever indicated by the pH of the neutral red indicator. This was on an average of every 3 days.

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[3] White, P. R., Growth, 10: 231, 1946.

OBSERVATIONS

In White's medium, very little proliferation occurred, although the edges of the explant remained clear and appeared to be viable (fig. 2, *A*). The addition of autologous serum to the medium resulted in some slight proliferation, although the cultures never became stabilized. During the first 24 hours there was a minimal amount of sloughing and rounding of the edges of the explants. In the cultures containing equal parts of autologous serum and White's medium, the proliferation began after this 24 hour period. It was noted that multiple stalk-like sheets of epithelium appeared which, within the next 24 to 48 hours, proliferated to a point where they curved toward one another, forming a bridge effect around the periphery of the culture (fig. 2, *B*). A minimal amount of fibrocytic proliferation was noted. The cells very often presented huge nuclei and pseudopodia. No definite tubular formation was noted. In a previous report we had observed the presence of large multinucleated cells in the urines collected from kidneys containing carcinoma. At that time we were uncertain as to whether these were neoplastic cells or were associated with hypernephroma. It has been suggested that they represented proliferating tubular cells. In stained preparations of the cultures, many multinucleated giant cells similar to those seen in the urinary sediment were observed. It is not contended that the multinucleated cells in the urinary sediment are malignant, but the similarity is made as a matter of record.

In previous attempts to grow this neoplasm in tissue cultures, using balanced salt solution, chick embryo juice and human placental cord serum, almost pure fibrocytic growth has resulted. It was not until autologous serum was used that an apparent suppression of fibrocytic growth occurred and epithelium grew out.

CONCLUSIONS

Carcinoma of the kidney has been cultivated in equal parts of autologous serum and White's medium, and its growth pattern described. White's medium alone (with rooster plasma coagulum) maintains carcinoma of the kidney, but does not support active growth.

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ABNORMAL RENAL MOBILITY

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Abnormal downward excursions of the kidney have been recognized and discussed by physicians for generations. The urologist has concerned himself with the problem of the correct management of this condition for many years. This subject has led to heated debates in the past, and differences of opinion as to the indications for and the techniques of treatment still exist.

Before the problem was well understood, patients with movable kidneys were operated upon for a variety of reasons and often without relief of symptoms. No surgical procedure attains 100 per cent results, and there is no more unhappy patient than the one who expects and fails to get complete relief after submitting to major surgery. By reviewing and re-evaluating past clinical experiences, a better perspective of the problem has been gained. By such study, the clinician has learned to select meticulously those cases for surgery in which there is reasonable assurance of improvement or cure.

Two hundred and forty-one cases of abnormal renal mobility, seen over a period of 5 years, are reviewed here. The normal kidney has an average range of motion up to 5 cm.; those exceeding this arbitrary limit are considered to have unusual mobility.

Two hundred and thirty-six were females; 5 were males.

The age groups are as follows:

	Number
15–20 yrs.	10
21–30 yrs.	74
31–40 yrs.	57
41–50 yrs.	38
51–60 yrs.	36
61–70 yrs.	18
71 + yrs.	8

The right kidney alone was involved in 201 patients; the left alone in 6; and the condition was bilateral in 34 patients.

The complaints presented by these patients are many and varied:

Presenting Complaint	*Number*
Frequency	39
Burning, urgency of urination	37
Hematuria	4
Incontinence (stress)	3
Dull, dragging pain, lumbar area	32
Intermittent flank pain, radiating to groin	14
Mass in abdomen	2
Abdominal discomfort, mild pain	21
Nausea	5
Back pain	25

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Low pain in back	8
Edema	2
Headache, hypertensive symptoms	3
Nervousness, loss of weight, fatigue and symptoms not referable to the urinary tract	46

The following associated conditions were also found in these patients:

Urological

Condition	*Number*
Hydronephrosis of pregnancy	1
Hydronephrosis with renal calculi	2
Pyelonephritis	3
Renal calculi	2
Renal tuberculosis	1
Diabetes mellitus with infected kidneys	2
Aneurysm of renal artery	1
Cystitis and urethritis	47

Nonurological

Condition	*Number*
Acute appendicitis	1
Carcinoma of the uterus	3
Gall stones	2
Spondylolisthesis	2
Arthritis of lumbar vertebrae	7
Pelvic inflammatory disease	5
Multiple myeloma	1
Hodgkin's disease	1

Positive urine cultures were found in 27 patients, although kidney specimens were not obtained on all patients.

ORGANISM	KIDNEY	BLADDER
Non-hemolytic streptococcus	1	3
B. aerogenes	1	4
B proteus		1
B pyocyaneus	1	1
B coli	6	18

Surgery was performed on 33 patients of this group of 241. Nephrectomy was done for a case of renal tuberculosis associated with a small aneurysm of the renal artery. Another nephrectomy was performed at the written request of the patient who had a moderate hydronephrosis. A pelviolithotomy was combined with nephropexy in another case. The remainder, 30 cases, had nephropexy with partial renal sympathectomy. Eight of the patients who underwent operations had bacterial infections of the urinary tract.

A survey by questionnaire was made of the 30 patients who had had nephropexies to determine the ultimate results. The results of this survey are as follows:

Complete relief of symptoms	14
Marked improvement, occasional mild symptoms	9
Some improvement, persistent mild symptoms	3
Recurrence of symptoms (x-rays normal)	1
Unable to obtain follow-up report	3

The mere presence of abnormal renal mobility does not imply altered renal physiology or perirenal disease. The freely mobile kidney is very often a physiologically normal organ, and the degree of descent does not determine pathological changes. The actual mobility is unimportant compared to its effect on the ureter. A kidney may have only a slightly abnormal excursion and yet produce both symptoms and demonstrable evidence of pyelorenal damage. To produce pathological changes, the ptotic kidney must be subject to some obstruction resulting in hydronephrotic changes—or infection as a result of stasis. It must be mentioned that in some instances, nephroptosis is merely part of the picture of generalized visceroptosis, and that these movable kidneys rarely are the cause of symptomatology.

Because nephroptosis does not produce symptoms in most cases, it is impossible to assign to it any characteristic symptom complex. A common symptom noted by the patient is a dull persistent pain in the lumbar area. This frequently has a postural relationship, increasing during fatigue or prolonged periods in the erect position and is often relieved by rest in bed. The pain is constant in its location, and the patient usually can consistently define the area of pain with the hand. Gastro-intestinal symptoms vary, and vomiting is not the rule. In a few cases, colic may occur suddenly, accompanied by severe pain in the kidney region with radiation down the ureter. In these instances, vomiting may occur. Symptoms referable to the bladder are inconstant unless an associated infection is present. Digestive disturbances with symptoms simulating conditions of the gastro-intestinal tract may be reflex manifestations of the disease but are far from pathognomonic.

The diagnosis of nephroptosis can be made easily. However, if we are to avoid the pitfalls of nephropexy, the greatest judgment must be exercised in selecting cases for surgical treatment. A thorough urological investigation as well as a comprehensive general study of the patient is indicated, and only after careful interpretation of the findings, can we predict the advisability of surgery. Nephroptosis, per se, rarely indicates disease. Pathological changes as evidenced by delay in emptying of the pelvis or dilatation of the pelvio-calyceal system should be demonstrable. Unusual downward excursions of the kidney are frequently found by bimanual palpation of the abdomen. The excretory urogram, however, is perhaps the most valuable procedure in making an accurate diagnosis. A series of films in the erect and recumbent positions may yield much information relative to renal function, pyelographic changes, and the emptying ability of the pelvis and ureter. Pyelectasis and calyectasis can be more accurately interpreted by this method than by retrograde filling. In a few instances, we have attempted to evaluate a questionable atonic pelvis by repeating the urograms after the patient had been up and about for some time or by keeping the patient erect during the entire excretory study. We have also repeated this procedure during episodes of pain. To date, however, it has not provided much additional information.

If the urograms are incomplete or inconclusive, retrograde studies are in order. Films following removal of the catheters should be taken at 5 and 10 minute intervals, and possibly later, to determine trapping of the opaque dye in the pelvis. Pyelo-ureterograms should also be made to ascertain the status of the ureters. During retrograde filling, the patient's pain is occasionally reproduced, and this may be significant but not conclusive evidence indicating that the kidney is the source of the patient's complaint.

The patient with nephroptosis is never an urgent surgical case. In noninfected nephroptosis, we further test these people with a garment or some form of postural therapy to determine if keeping the kidney in its normal position produces symptomatic relief. Where there is the slightest doubt regarding the clinical significance of the nephroptosis, we prefer to observe these patients over a period of time and repeat the studies before deciding to operate.

Many and varied symptoms have been ascribed to the freely movable kidney. In evaluating the patient's symptoms, all possible causes of disturbance other than renal mobility must be considered. If we focus too sharply on the descended kidney and dimly view the rest of the patient, errors in treatment may result. Each system must be investigated with suspicion. Careful consideration must be given to the patient's nervous system. Symptoms caused by functional disturbances of the nervous system can closely simulate those of organic origin. Symptoms are frequently magnified by the unstable and neurotic individual. Unless the utmost care is exercised, these patients will grasp at any suggestion of an organic lesion and readily submit to surgical treatment if it is suggested. The patient with the well-scarred abdomen deserves considerable contemplation before surgery.

Lesions of the musculoskeletal system may produce symptoms which are often misleading and difficult to diagnose. Patients with backache, believing they have kidney trouble, frequently seek aid from the urologist. Backache must always draw attention to the many possible orthopedic causes.

For those vague complaints of a gastro-intestinal nature such as indigestion, nausea, and gas, we can ill afford to forget the viscera contained within the peritoneum. X-ray visualization of the biliary and gastro-intestinal tract may be necessary to exclude disease in each system. Critical study is essential if surgical treatment is to be properly applied.

INDICATIONS

We believe that surgery is indicated to correct or remove pathological conditions. Operative treatment should be reserved for those patients in whom careful study has definitely established the ptosed kidney as the cause of the complaints. Where there are signs of obstruction with pelviorenal damage or delay in emptying the pelvis, operative treatment is indicated. If an abnormally movable kidney is the site of repeated recurrent infections, despite conservative treatment with a garment and proper antibacterial agents, surgical correction may be considered. Nephropexy should be beneficial to the occasional patient who suffers severe episodes of renal colic or so-called Dietl's crises. Some patients have worn a garment for years with satisfactory relief of symptoms; others become tired of applying and wearing the belt. Nephropexy is advocated for these individuals.

Any operative procedure to correct difficulties due to nephroptosis must be designed to hold the kidney in its normal position, provide free urinary drainage, and avoid damage to the renal parenchyma. It would be heedless to fix the kidney itself without correcting the frequently associated lesions of the ureteropelvic area. We believe that a simple technique which will attain these objectives will be successful. In our practice, the kidney is dissected free from all perirenal tissue. The ureter is also freed for a considerable distance. All bands of tissue that may impair drainage are removed. Particular attention is given the ureteropelvic junction so that there is no mechanical interference with pelvic emptying. The pedicle is also dissected free of adherent tissue, and the sympathetic fibers are interrupted. We realize that this is only a partial sympathectomy, but we have felt the procedure useful even though the ultimate results of this procedure are not clearly understood. We frequently hammock the kidney by suturing the peri-renal fascia according to the Deming technique. After surgery, a pressure pad is applied to the corresponding hypogastrium. The foot of the bed is elevated for 72 hours. The patient is usually up in 10 days and is checked postoperatively with urograms. The patient is sent home 2 weeks following surgery and advised to avoid any strenuous exercise for a month. After a 3 month period, a recheck examination is made, and if the urograms are satisfactory, the patient is discharged.

SUMMARY

Renal ptosis as an uncomplicated entity is rarely an indication for surgery. The movable kidney may be the abdominal mass which disturbs the patient's equanimity, but it would seem that under all ordinary circumstances, reassurance is more to the point than nephropexy. When nephroptosis, by virtue of angulation and obstruction of the ureter or ureteropelvic junction, is an underlying cause or a contributing factor in the production of urinary stasis, it becomes important to suspend the kidney. The one feature of nephroptosis which to a large degree defies satisfactory analysis is the factor of pull or drag on the renal pedicle.

In evaluating a series of 241 cases in which there was demonstrable nephroptosis, a reasonably rigid selection of cases has resulted in surgical treatment in 33 instances, of which 30 consisted of nephropexy with partial renal denervation. Follow-up survey of these 30 cases has shown that the overwhelming majority of such patients have been accorded real and welcome relief from symptoms.

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THE PRINCIPLE OF AORTIC COMPRESSION IN THE MANAGEMENT OF MASSIVE HEMORRHAGE FROM THE RENAL PEDICLE AFTER NEPHRECTOMY

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Loss of control of the renal pedicle during the course of nephrectomy is a hazard which faces every renal surgeon The difficulties of adequate exposure and dissection of the renal vessels are probably greatest when a large tumor of the kidney is approached through the flank Not only does the mass and limited mobility of the tumor tend to obscure the operator's view of the hilum, but the length of the pedicle is frequently greatly reduced The application of clamps or ligatures to the hilar vessels is all too often a blind procedure guided only by palpation If, after the tumor is removed, an insecure ligature or clamp slips, the ensuing severe hemorrhage may be controllable only by rapid packing or by digital compression While pressure for a few minutes may permit subsequent isolation and ligation of the bleeding vessels, occasionally the hemorrhage may be so profuse that permanent packing must be used At times a clamp applied to short vessels must be left in the wound Both the pack and the clamp are temporizing measures which, although occasionally effective for permanent hemostasis, may merely postpone exsanguination until subsequent removal

Since 1916, over 1000 nephrectomies have been carried out through the flank at the Brady Urological Institute of the Johns Hopkins Hospital Four deaths occurred due to hemorrhage from the renal pedicle in this group of patients In two instances the ligatures slipped from the vessels as the clamps were being released One of these patients, who was operated on in the days before blood banks, died on the table from hemorrhage, the wound of the other was packed, but the patient died 3 days later from hemorrhagic shock In a third case, the pedicle was divided and ligated without incident and the flank wound was being closed when massive bleeding occurred After a futile search for the open vessel, the wound was packed and the patient was returned to the ward where he survived for about 12 hours In the last case, the pedicle was lacerated by a transfixion suture after it had been securely clamped Severe bleeding ensued which was finally controlled by clamps which were placed on the pedicle and left in the wound, however, the patient died in shock within 24 hours

These temporary compressive measures are extremely unreliable at best for permanent occlusion of large vessels Having been confronted recently with the problem of massive bleeding from the renal pedicle which could not be controlled by packing, we have devised a technique which permits visualization and closure of the open vessels

OPERATIVE TECHNIQUE

The technical plan for direct visualization and closure of the bleeding renal vessels is based on temporary packing of the flank wound, an extensive transperitoneal exposure, and temporary occlusion of the abdominal aorta above the origin of the renal arteries. While this plan is applicable to the control of bleeding from either renal pedicle, the details of the procedure (fig. 1) in the management of bleeding from the right renal pedicle will be described.

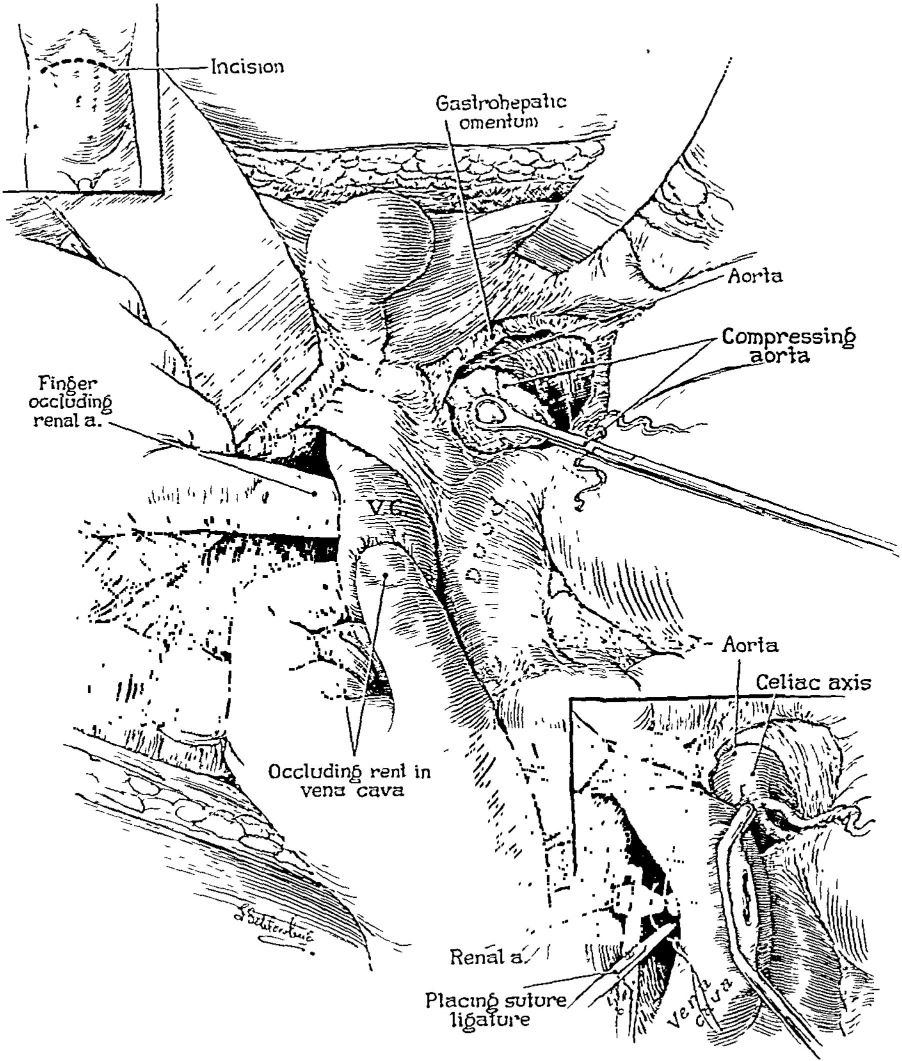

FIG. 1. Technical steps in management of massive hemorrhage from renal pedicle after nephrectomy. Suture of rent in vena cava may be accomplished while edges of defect are compressed manually. Lower insert shows alternate method with use of partial occlusion clamp on vena cava.

The anesthetized patient is placed on the operating table in supine position with the right side somewhat elevated. Cannulae are inserted into two or more veins and blood is started immediately. The right flank and entire abdomen are prepared and draped. A transverse upper abdominal incision is placed which

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Loss of control of the renal pedicle during the course of nephrectomy is a hazard which faces every renal surgeon. The difficulties of adequate exposure and dissection of the renal vessels are probably greatest when a large tumor of the kidney is approached through the flank. Not only does the mass and limited mobility of the tumor tend to obscure the operator's view of the hilum, but the length of the pedicle is frequently greatly reduced. The application of clamps or ligatures to the hilar vessels is all too often a blind procedure guided only by palpation. If, after the tumor is removed, an insecure ligature or clamp slips, the ensuing severe hemorrhage may be controllable only by rapid packing or by digital compression. While pressure for a few minutes may permit subsequent isolation and ligation of the bleeding vessels, occasionally the hemorrhage may be so profuse that permanent packing must be used. At times a clamp applied to short vessels must be left in the wound. Both the pack and the clamp are temporizing measures which, although occasionally effective for permanent hemostasis, may merely postpone exsanguination until subsequent removal.

Since 1916, over 1000 nephrectomies have been carried out through the flank at the Brady Urological Institute of the Johns Hopkins Hospital. Four deaths occurred due to hemorrhage from the renal pedicle in this group of patients. In two instances the ligatures slipped from the vessels as the clamps were being released. One of these patients, who was operated on in the days before blood banks, died on the table from hemorrhage; the wound of the other was packed, but the patient died 3 days later from hemorrhagic shock. In a third case, the pedicle was divided and ligated without incident and the flank wound was being closed when massive bleeding occurred. After a futile search for the open vessel, the wound was packed and the patient was returned to the ward where he survived for about 12 hours. In the last case, the pedicle was lacerated by a transfixion suture after it had been securely clamped. Severe bleeding ensued which was finally controlled by clamps which were placed on the pedicle and left in the wound; however, the patient died in shock within 24 hours.

These temporary compressive measures are extremely unreliable at best for permanent occlusion of large vessels. Having been confronted recently with the problem of massive bleeding from the renal pedicle which could not be controlled by packing, we have devised a technique which permits visualization and closure of the open vessels.

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and the pedicle was divided between the two distal clamps. After the kidney was removed it was possible to see that the pedicle was very short and that the two pedicle clamps contained a moderate amount of hilar fat in addition to the vessels. A ligature was passed behind the proximal clamp and as it was tied both clamps were dislodged and profuse bleeding ensued. This was temporarily controlled by pressure with a laparotomy pad. Repeated efforts to expose and clamp the vessels were unsuccessful and resulted in severe blood loss. Finally, the renal fossa was packed tightly with a gauze roll and the wound was closed. There was no evidence of further blood loss. Except for moderate abdominal distention the immediate postoperative course was uneventful.

Nine days later the patient was again taken to the operating room for removal of the pack. The incision in the flank was reopened and the pack was slowly freed. Massive bleeding occurred as the last portion of pack was withdrawn. Several attempts were made to visualize and clamp the vessels in the depths of the flank wound. The severe bleeding, however, filled the wound so rapidly and persistently that attempts to secure the pedicle were abandoned, another pack was inserted tightly, and the wound was closed. After blood replacement the patient's condition remained stable, the bleeding again seemed to be controlled by the pack and the course was uneventful for the next week.

On July 8, 1951, 18 days after the nephrectomy, the patient suddenly began to bleed profusely around the pack and immediately went into shock. After reinforcement of the packing material and several transfusions, he was again taken to the operating room where the plan just outlined was put into effect. Under pentothal anesthesia, cannulae were inserted into 3 veins and blood was started. A transverse upper abdominal incision was placed, both recti were divided and the peritoneum opened widely. A huge mass consisting of hematoma and the gauze pack occupied the retroperitoneal space in the region of the right renal fossa. A rent was made in the gastrohepatic ligament, the abdominal aorta at the level of the celiac axis was identified and a sponge in the grasp of a heavy sponge forceps was placed in readiness on the aorta. The hepatic flexure was reflected downward and loops of bowel were packed out of the subhepatic fossa. The posterior peritoneum was incised and the descending duodenum was mobilized and retracted medially. The abdominal aorta was then occluded by forceful compression against the spine. The huge hematoma was entered directly and evacuated manually. Profuse venous bleeding came from a round hole in the vena cava representing the site of avulsion of the right renal vein. The bleeding was controlled quickly by compression of the margins of the caval opening between the operator's thumb and forefinger. A weak arterial stream could then be identified coming from behind the cava. This was readily controlled by more forceful compression of the abdominal aorta and by digital pressure locally. While assistants maintained aortic compression and digital pressure over the renal artery the operator closed the opening in the vena cava with a continuous suture of 4-0 arterial silk. The Satinsky clamp which was in readiness was not required. The sutured vena cava was retracted medially, the stump of the renal artery was readily identified and transfixed and extends from the lateral aspect of the costal margin on the right to a similar point on the left. Both rectus muscles are divided and the wound is opened to its full extent. The gastrohepatic ligament is incised and the abdominal aorta at the level of the celiac axis is identified by palpation. The aorta is occluded at this point by forceful compression against the vertebral column. (Complete occlusion of the aorta by manual compression is difficult and compressive occlusion is facilitated by the use of a "stick sponge" or a folded gauze pad in the grasp of a heavy sponge forceps.) The hepatic flexure of the colon is mobilized and reflected downward. The posterior peritoneum along the descending duodenum is incised and the latter retracted medially. The hematoma in the renal fossa is then entered and evacuated manually and by the use of suction. Venous bleeding from the orifice of the renal vein is identified and the stump of the renal vein or rent in the vena cava is secured by the operator's thumb and forefinger. Suture of the venous opening, if small, may be accomplished at once while manual compression of its edges is maintained by the operator's thumb and forefinger. If a large rent in the cava exists, a partial caval occlusion clamp *such as that designed by Satinsky*[1] *may be applied and the defect* closed by suture. A continuous over and over suture of 4-0 or 5-0 arterial silk on an atraumatic needle is satisfactory.

The vena cava is then retracted medially and the stump of the right renal artery is identified. Removal of the pack in the flank wound may improve exposure at this point. The open artery is securely transfixed and ligated. If the renal artery has been torn out of the aorta the latter may be exposed by further medial retraction of the vena cava and the aortic defect closed with continuous or interrupted sutures of 4-0 arterial silk.

After closure of the defects in the vessels aortic compression is released. The opening in the posterior peritoneum is closed loosely and the omentum is brought over this area. The abdominal incision is closed in layers with interrupted silk sutures. A drain is placed in the flank wound and the latter is closed loosely to the drain. The technical steps in this procedure are sketched in the accompanying figure. Its successful application is illustrated by the following clinical report.

CASE REPORT

V. G. (J. H. H. No. 574760), a 55 year old white man, was admitted to the Brady Urological Institute of the Johns Hopkins Hospital on June 12, 1951 with a 6 month's history of hematuria. Urological investigation revealed the presence of a large mass in the right renal pelvis which obstructed the upper calyx. A diagnosis of carcinoma of the renal pelvis was made and a right nephroureterectomy was planned. At operation on June 15, 1951 the kidney was exposed through an incision in the right flank. Mobilization was difficult and was never satisfactory because of a short pedicle. This was partially obscured by the large tumor which occupied the renal pelvis. Two renal pedicle clamps were applied by palpation, a smaller curved clamp was placed adjacent to the kidney and the pedicle was divided between the two distal clamps. After the kidney was removed it was possible to see that the pedicle was very short and that the two pedicle clamps contained a moderate amount of hilar fat in addition to the vessels. A ligature was passed behind the proximal clamp and as it was tied both clamps were dislodged and profuse bleeding ensued. This was temporarily controlled by pressure with a laparotomy pad. Repeated efforts to expose and clamp the vessels were unsuccessful and resulted in severe blood loss. Finally, the renal fossa was packed tightly with a gauze roll and the wound was closed. There was no evidence of further blood loss. Except for moderate abdominal distention the immediate postoperative course was uneventful.

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[1] Satinsky, V. P.: Thoraco-abdominal approach for portacaval anastomosis. Ann. Surg., **128**: 938, 1948.

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Pathological examination of the right kidney showed a papillary carcinoma of the renal pelvis. The patient has been followed for 3 months and has shown no ill effects from the temporary aortic compression.

COMMENT

It is beyond the scope of this report to discuss the various techniques which have been described for ligation of the renal vessels in the performance of nephrectomy. Suffice it to say that careful exposure and dissection of large vessels prior to their interruption is a sound surgical principle of general application. Blind clamping and mass ligation of large undissected vascular pedicles are to be deplored and is probably associated with an incidence of catastrophe approaching that which accompanied pulmonary resection with the hilar tourniquet before the advent of modern dissection techniques.

When control of the pedicle is lost during nephrectomy, Rathbun advocates gauze tamponade with compression of the vessels against the spine; the pedicle is approached from above and secured under direct vision.[2] Most injuries to the duodenum, pancreas, adrenal or colon during nephrectomy have been due to the blind application of clamps in a bloody field.[3, 4, 5, 6] If control of the pedicle can not be regained under direct vision by Rathbun's method, it is our opinion that the renal fossa should be packed tightly and the procedure which has been described above be carried out at once. It would seem highly advantageous to perform an immediate closure of the bleeding vessels since to rely on packing alone is to expose the patient to the risk of serious late hemorrhage.

Aside from the advantage of a wide transperitoneal exposure the important principle in this procedure is that of control of arterial bleeding by occlusion of the abdominal aorta proximal to the origin of the renal arteries. Aortic occlusion might be theoretically more complete if the aorta were to be dissected out

[2] Rathbun, N. P.: Some of the accidents of renal surgery. J. Urol., **20:** 427, 1928.

[3] Goldstein, A. E.: Accidents in renal surgery. Surg., Gynec. & Obst., **65:** 515, 1937.

[4] Young, H. H. and Davis, D. M.: Young's Practice of Urology, Philadelphia: W. B. Saunders Co., 1926.

[5] Ockerblad, N. F. and Carlson, H. E.: Accidents in renal surgery. South. Med. J., **34:** 899, 1947.

[6] Hyman, A. and Leiter, H. E. Surgery of the inferior vena cava in urologic conditions. J. Urol., **45:** 813, 1941.

and grasped with a non-crushing clamp. However, the abdominal aorta proximal to the origin of the right renal artery lies between the crura of the diaphragm. Its position and the presence of the celiac axis and its branches make this a difficult and hazardous dissection. Occlusion of the aorta in this area can be accomplished quickly and easily by forceful compression against the spine and this maneuver is better adapted as an emergency measure. The principle of proximal aortic compression in the control of profuse arterial hemorrhage is applicable to a wide variety of situations.

SUMMARY

A technique is described for management of massive hemorrhage from the renal pedicle after nephrectomy which consists of temporary packing of the renal fossa, a wide transperitoneal exposure, compression of the abdominal aorta above the origin of the renal arteries and direct visualization and closure of the bleeding vessels.

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MONILIAL INFECTION OF THE KIDNEY: CASE REPORTS

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This report was prompted by the apparent rarity of this type of infection and the recent emphasis by Wood et al. on monilial infections in other parts of the body complicating the use of antibiotics. Two cases illustrating many features of this type of infection are reported, along with a discussion of literature, laboratory aspects, pathogenicity, and therapy.

CASE REPORTS

Case 1. A 28-year-old white woman entered for urologic study on April 15, 1951. She complained of pain in the right renal area and chronic pyuria. Attacks of moderately severe aching pain had occurred on the average of once a week for over six months. The pyuria could not be eradicated by any of the common antibiotics although the urine could be freed of the gram-negative bacteria. She only rarely had a low-grade fever. She had had a right pelviolithotomy a year previously at which time she had received much antibiotic therapy including chloromycetin. Past history revealed congenital syphilis, adequately treated, and rheumatic fever. Physical examination was essentially negative except for tenderness in the right costovertebral angle and mitral regurgitation which was considered to be due to rheumatic fever.

Laboratory tests excluding the urinary studies and a positive serology were essentially normal. At the time of her first visit microscopic examination of a centrifuged specimen of urine showed 50 pus cells per high power field and an occasional gram-negative bacillus and yeast cell. Two grams of triple sulfa (sulfadiazine, sulfamerazine, and sulfamethazine) daily were prescribed. Culture of the urine revealed a pure growth of a yeastlike organism which on adequate study proved not to be monilia albicans but a monilia of unknown species. The same yeastlike organism was found in a culture of a catheterized specimen of urine on May 2, 1951, and on May 8, 1951.* The organism seemed to grow more abundantly after she had taken a considerable amount of triple sulfa. The gram negative rod was no longer found in urine stained by Gram's method. On May 3, 1951, an excretory urogram revealed rather marked calyectasis on the right with recurrent formation of a calculus and an essentially normal-appearing pelvis. The left kidney appeared normal. Cystoscopy revealed very mild, diffuse, chronic cystitis, although she had no symptoms referable to the lower part of the urinary tract. The specimen of urine from the left kidney was entirely negative, that from the right revealed 15 to 20 pus cells per highpower field and a pure culture of the same monilia In view of the rheumatic heart disease, recurrent stone formation, pain,

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Read at annual meeting, South Central Section, American Urological Association, Houston, Texas, October 31, 1951.

* Laboratory studies for monilia on the patients reported in this paper were carried out with the consultation of Dr. Homer Marsh, Professor of Bacteriology, at the University of Oklahoma Medical School.

persistent calyectasis and pyuria, nephrectomy was advised. It was felt that the yeast infection was possibly superimposed on an underlying chronic renal infection.

Nephrectomy was carried out on May 16, 1951, and convalescence was uneventful. She was dismissed from the hospital on the seventh postoperative day. Repeated urinalyses during the postoperative period have continued to be negative for monilia, the last examination of the urine being done on August 11, 1951. Examination of the excised kidney disclosed infected hydronephrosis with calculus formation. There was no evidence of invasion of the renal parenchyma by the fungi. The same monilial species was found in cultures from the urine in the calyces.

Case 2. A 53-year-old white woman was first seen on March 23, 1951 complaining of symptoms referable to the left kidney since 1936, at which time she had had painful hematuria and was told she had passed a stone. She experienced mild recurring episodes of pain in the left costovertebral angle until the early part of 1951 at which time the attacks became more frequent. They were more severe, resembled renal colic and were associated with pyuria.

Physical examination revealed a moderate degree of tenderness in the left costovertebral angle. Mild anemia (red blood cells, 3,900,000) was noted and the other laboratory tests were within normal limits except for the urinary findings. Microscopic examination of the sediment of a catheterized specimen of urine revealed 40 pus cells per high power field and examination of the urine stained by Gram's method revealed gram-negative bacilli and rare yeast cells. An excretory urogram on March 23, 1951, disclosed an essentially normal right kidney with mild dilatation of the lower ureter. Minimal inflammatory changes with a questionable filling defect of the pelvis of the left kidney and dilatation of the lower portion of the ureter were noted. Cystoscopy disclosed mild cystitis. A specimen of urine from the right kidney was negative, microscopically and by means of culture. Urine from the left kidney contained 10 to 20 pus cells per high power field and gram-negative bacilli which by cultural means were shown to be Proteus (species?). The left retrograde pyelogram again suggested a filling defect of the pelvis (fig. 1, *A*). The left kidney was re-examined a few days later and the apparent filling defect could not be demonstrated (fig. 1, *B*). It was thought best to carry out conservative therapy for the time being and 2 gm. of sulfa daily was prescribed. The pyuria decreased and the gram-negative bacilli disappeared from the urine, yet the pain persisted in the left kidney. On May 15, 1951 she experienced an attack of severe pain in the left kidney with nausea and vomiting. On May 17, 1951 a left pyelogram appeared as before, showing only mild inflammatory changes. The specimen of urine from the left kidney revealed marked pyuria, numerous yeast cells and a few gram-negative bacilli. The specimen of urine from the right kidney was negative. It was decided to treat the infection with chloromycetin to see if the pain could be relieved if the infection was controlled. Chloromycetin appeared to aggravate her condition and the pyuria increased. After 4 days of chloromycetin therapy, she felt something pass from the left kidney and recovered a whitish membrane in the form of a wrinkled mass 2 cm.

in diameter from her urine. She fortunately collected and saved this specimen of urine. It was loaded with fungi but contained no bacteria. It was apparent that the monilial infection had become worse with chloromycetin therapy and it was discontinued after five days. Repeated examinations of catheterized specimens of vesical urine revealed monilia (fig. 2) which on culture proved to be Monilia albicans. Microscopic studies of sections of the voided membrane were reported as strands of keratin with adult type squamous epithelial cells which suggested leukoplakia of the pelvis. Another retrograde study was performed on June 1, 1951, after the membrane had been passed, which revealed numerous filling de-

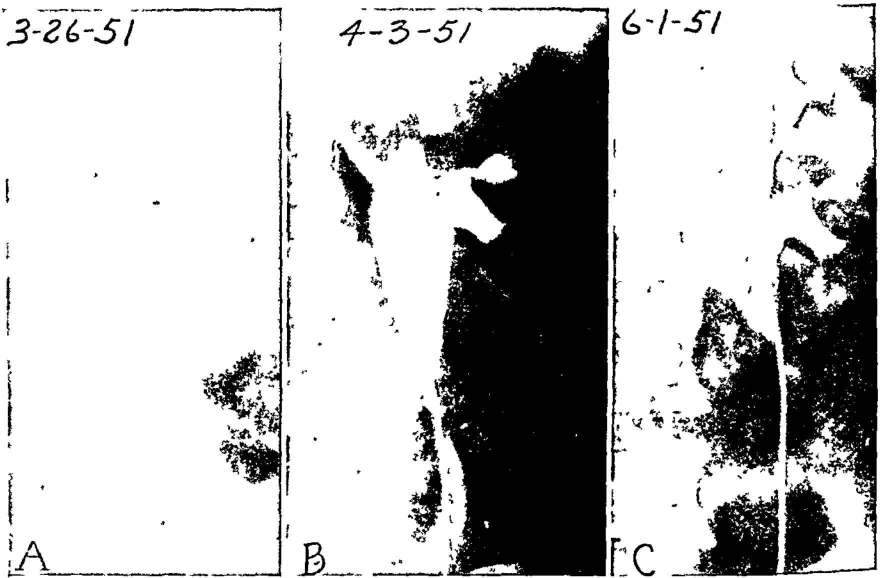


Fig. 1. Case 2. *A*, left retrograde pyelogram showing apparent filling defect. *B*, left retrograde pyelogram a few days later seeming to rule out filling defect. *C*, left retrograde pyelogram soon after membrane was voided showing ragged borders and filling defects of pelvis.

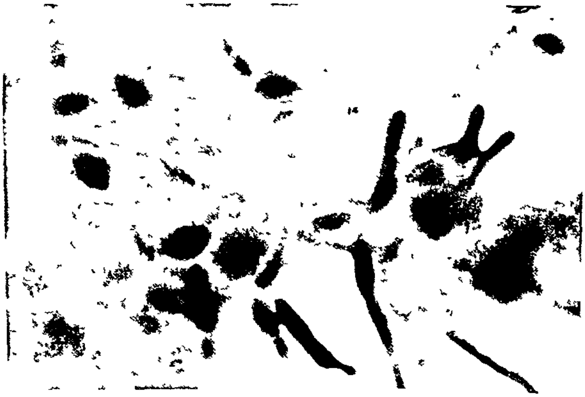


Fig. 2. Case 2. Gram stain showing spores and mycelia of monilia with pus cells in background under oil emersion.

fects in the pelvis (fig. 1, *C*). A diagnosis of leukoplakia of the left renal pelvis was made and nephrectomy advised. Large doses of vitamin B_1 were prescribed prior to surgery. On June 15, 1951, left nephrectomy was performed with some difficulty due to perinephritis, making it necessary to do a subcapsular nephrectomy. Grossly the kidney showed extensive leukoplakia in the pelvis and chronic pyelonephritis. Microscopic studies verified the diagnosis of leukoplakia and chronic pyelonephritis. Monilia albicans was cultured from the urine in the calyces but could not be seen in the tissue sections.

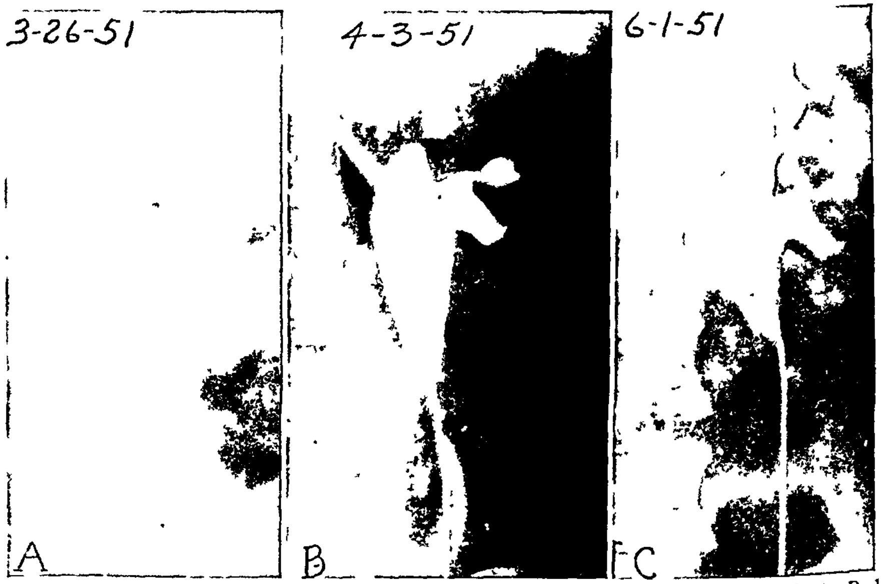
The postoperative course was entirely uneventful and she was dismissed from the hospital on the eighth postoperative day. Examination of the urine for fungi yielded negative results and the urine contained only a few pus cells from the fourth postoperative day to the sixteenth postoperative day in spite of the absence of chemotherapy. On the last day of June mild pyuria with an absence of organisms was found. Triple sulfa was prescribed and on July 10 the urine contained more pus cells and Monilia albicans. At this time it was deemed advisable to stop all antibacterial therapy and to treat the fungus infection. This was attempted with irrigations of the bladder and left ureteral stump with 1:10,000 gentian violet every third day for four treatments and the oral administration of Lugol's solution, 15 drops three times daily for three weeks. She improved somewhat but noted vesical symptoms while receiving local therapy; a week following discontinuance of local treatment she felt perfectly comfortable although the urine continued to contain monilia and pus. Alkalinization of the urine only was continued for 6 weeks. At the end of this time the urine contained no monilia but a return of gram-negative bacilli (Aerobacter aerogenes) was noted. Without treatment, urine findings remained unchanged for several weeks while she continued to be essentially asymptomatic. Early in October a triple sulfa, 2 gm. daily, was prescribed to see if the monilia would return. In 1 week the gram-negative bacillus disappeared and monilia was found in the bladder urine. The pyuria decreased from about 40 to 20 cells per high power field. Retrograde studies failed to implicate the ureteral stump as the focus of this infection. Cultures from the right ureter and bladder were positive for monilia; however, the right ureteral specimen was negative microscopically. Due to the lack of symptoms, further therapy may not be indicated but combined antibacterial and antimonilial therapy is contemplated.

It should be added that concentrated 24-hour specimens of urine cultured for tuberculosis were negative in both of these cases and vaginal examinations revealed no monilia or abnormal secretion.

DISCUSSION

In view of the fact that these 2 cases were encountered over a short period of time, and the relationship of monilial infections to antibiotic therapy has been emphasized in other parts of the body, the report of these cases seemed timely. General texts on urology as well as pathology give meager, if any, information on this particular subject.

Moulder, in 1946, reported a case of cystitis due to monilia and reviewed the in diameter from her urine. She fortunately collected and saved this specimen of urine. It was loaded with fungi but contained no bacteria. It was apparent that the monilial infection had become worse with chloromycetin therapy and it was discontinued after five days. Repeated examinations of catheterized specimens of vesical urine revealed monilia (fig. 2) which on culture proved to be Monilia albicans. Microscopic studies of sections of the voided membrane were reported as strands of keratin with adult type squamous epithelial cells which suggested leukoplakia of the pelvis. Another retrograde study was performed on June 1, 1951, after the membrane had been passed, which revealed numerous filling de-



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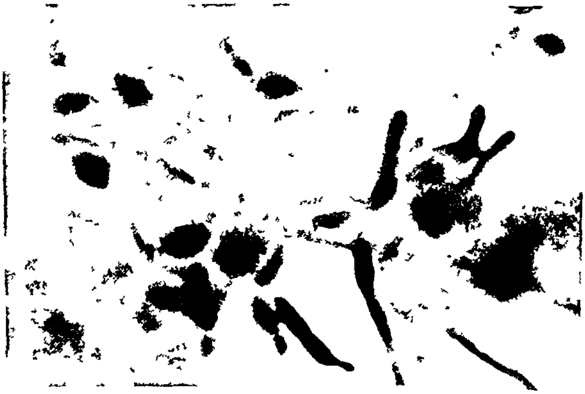

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fects in the pelvis (fig. 1, *C*). A diagnosis of leukoplakia of the left renal pelvis was made and nephrectomy advised. Large doses of vitamin B_1 were prescribed prior to surgery. On June 15, 1951, left nephrectomy was performed with some difficulty due to perinephritis, making it necessary to do a subcapsular nephrectomy. Grossly the kidney showed extensive leukoplakia in the pelvis and chronic pyelonephritis. Microscopic studies verified the diagnosis of leukoplakia and chronic pyelonephritis. Monilia albicans was cultured from the urine in the calyces but could not be seen in the tissue sections.

The postoperative course was entirely uneventful and she was dismissed from the hospital on the eighth postoperative day. Examination of the urine for fungi yielded negative results and the urine contained only a few pus cells from the fourth postoperative day to the sixteenth postoperative day in spite of the absence of chemotherapy. On the last day of June mild pyuria with an absence of organisms was found. Triple sulfa was prescribed and on July 10 the urine contained more pus cells and Monilia albicans. At this time it was deemed advisable to stop all antibacterial therapy and to treat the fungus infection. This was attempted with irrigations of the bladder and left ureteral stump with 1:10,000 gentian violet every third day for four treatments and the oral administration of Lugol's solution, 15 drops three times daily for three weeks. She improved somewhat but noted vesical symptoms while receiving local therapy; a week following discontinuance of local treatment she felt perfectly comfortable although the urine continued to contain monilia and pus. Alkalinization of the urine only was continued for 6 weeks. At the end of this time the urine contained no monilia but a return of gram-negative bacilli (Aerobacter aerogenes) was noted. Without treatment, urine findings remained unchanged for several weeks while she continued to be essentially asymptomatic. Early in October a triple sulfa, 2 gm. daily, was prescribed to see if the monilia would return. In 1 week the gram-negative bacillus disappeared and monilia was found in the bladder urine. The pyuria decreased from about 40 to 20 cells per high power field. Retrograde studies failed to implicate the ureteral stump as the focus of this infection. Cultures from the right ureter and bladder were positive for monilia; however, the right ureteral specimen was negative microscopically. Due to the lack of symptoms, further therapy may not be indicated but combined antibacterial and antimonilial therapy is contemplated.

It should be added that concentrated 24-hour specimens of urine cultured for tuberculosis were negative in both of these cases and vaginal examinations revealed no monilia or abnormal secretion.

DISCUSSION

In view of the fact that these 2 cases were encountered over a short period of time, and the relationship of monilial infections to antibiotic therapy has been emphasized in other parts of the body, the report of these cases seemed timely. General texts on urology as well as pathology give meager, if any, information on this particular subject.

Moulder, in 1946, reported a case of cystitis due to monilia and reviewed the literature up to that time. He mentioned the first case of renal moniliasis diagnosed during life as reported by Rafin in 1910. Rafin reported a case of vesical moniliasis in a woman with urinary tract tuberculosis in 1927. The other reports up to 1946 on the subject seem difficult to evaluate. Relative to Moulder's case it is interesting that he treated the patient with sulfathiazole, penicillin, silver nitrate, and gentian violet instillations, mapharsen and alkalinization with benefit only after 2 months' drug-free period, making it difficult to assess the value of any of the therapy. A biopsy of the bladder revealed keratinization suggesting the possibility of an early leukoplakia which is interesting in view of the leukoplakia in the second case just reported. Since this thorough report several cases of urinary tract moniliasis have been reported. Cozza reported a case of cystitis due to using an unsterile enema can for vesical lavage. This case responded rapidly to tryptoflavin. Snyder reported cystitis of 10 years' duration due to monilia with a thrushlike membrane, and with symptoms which he thought were due to other organisms present. Sauer and Metzner reported a case of marked cystitis and thrushlike lesions of the bladder which did not respond to sodium bicarbonate, gentian violet instillation, solution G, penicillin and streptomycin. After 5 months with no treatment the patient still had thrushlike membrane but no monilia in the urine. Rivas and De La Rosa reported a case of renal moniliasis associated with tuberculosis of the kidney and felt that all symptoms were due to tuberculosis. Engelhard reported a well-studied generalized Monilia albicans infection in a child. It involved the left ureter, bladder and urethra in the urinary tract. Recovery was considered spontaneous, although iodides, diet, and alkalinization of the urine were used.

Reports of renal moniliasis have been very rare, but if one considers the whole urinary tract some generalities can be made. Therapy has usually been ineffective. There is often question regarding the part the monilia plays in the patient's symptoms. The laboratory aspects of the diagnosis of Monilia albicans infections are usually lacking and when mentioned the diagnosis is usually made only by a study of smears of the urinary sediment. This makes the diagnosis of Monilia albicans infection questionable in many of the reported cases. It is probable that many cases of monilial infection of the urinary tract are not reported as such which is illustrated in the paper of Howard and Buchtel who mention a serious yeast infection in a child.

Monilia albicans is identified by finding terminal chlamydospores when the yeast is grown on corn meal agar at room temperature. Deep streaks are made in this medium which can easily be prepared or bought commercially. It sometimes must be held for weeks before the typical spores appear. Other species of monilia may form abundant mycelia and yeast cells quite identical with Monilia albicans but no chlamydospores. Monilia albicans is pathogenic in rabbits, usually killing them in 4–5 days following intravenous injection of a suspension of the organism.

In neither of the cases presented do we have any idea of the mode of infection. In case 1, infection could have happened at the time of previous surgery. In case 2, the possibility of contamination at the time of retrograde pyelographic study was considered although a rare yeast cell was reported in one of the first urines studied. In order to rule out contamination all our ureteral and several urethral catheters were carefully incubated in saline, the saline centrifuged and the sediment cultured. The results were negative. During this period numerous other patients were studied with the same equipment and no similar infections were produced.

The problem of enhancing monilia infections by the administration of aureomycin has been considered by many observers. Experimental in vitro work by Woods et al. failed to indicate any enhancement of this growth. However, Moore was able to show quite definitely that a dilute solution of aureomycin will stimulate the growth of monilia. It is usually considered that the added growth results from the elimination of other inhibiting organisms. In both patients the administration of triple sulfa and in the second case chloromycetin quite definitely caused exacerbation of the monilia infection.

The first patient in whose urine a species of monilia other than Monilia albicans was found probably did not suffer from the fungus even though it increased on sulfa therapy. In the case of the second patient whose urine contained Monilia albicans it appeared that this infection complicated her chronic renal disease. The part it played in the formation of the leukoplakia is, of course, unknown. The only time that it seemed to produce symptoms in this patient was when she was taking antibiotics to eradicate the gram-negative bacilli. During these periods she felt worse, had more pyuria and more renal pain. The clinical course of these patients confirmed the generally accepted opinion that only Monilia albicans is pathogenic.

It is interesting that treatment following nephrectomy was not necessary to eradicate the monilia from the urine of the first patient, which bears out the evidence for the saprophytic nature of her monilia. The second patient who had definite Monilia albicans was treated with gentian violet, Lugol's solution, alkalinization and vitamin B_1 without any immediate improvement. Only after prolonged alkalinization of the urine did the monilia disappear from the urine, but in its place was a gram-negative bacillus. However, this may indicate that alkalinization has some therapeutic value in Monilia albicans infections. From the literature and these cases it appears that Monilia albicans infection complicates chronic renal disease. Only after other cases of monilia infection proved by adequate cultural methods have been recognized and treated will the answer to this question be forthcoming. It is entirely possible that these infections will be more frequently encountered by urologists.

SUMMARY

Two cases of monilia infection of the kidney are reported, one due to a nonpathogenic monilia and one due to a pathogenic Monilia albicans. The literature, laboratory aspects, pathogenicity of the monilia, and therapy are covered in the discussion.

ADDENDUM

All therapy was discontinued December 1951, in the second patient presented. Study of the centrifuged urinary sediment has continued to reveal 8 to 10 pus cells per high powered field with a negative gram stain. Repeated cultures revealed only a decreasing number of colonies of Monilia albicans until May 1952, when they became negative and have remained negative for Monilia albicans on repeated cultures since. The patient has remained asymptomatic since last November, and an excretory urogram in March 1952, revealed essentially an unchanged right kidney.

A simplified technique for the identification of Monilia albicans described by Fusillo, Learnard and Dozier has made possible the diagnosis of Monilia albicans based on the production of terminal chlamydospores in 48 hours.

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INJURY OF THE KIDNEY IN CHILDREN

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The records of 45 children treated for a kidney injury during the past 40 years are the basis of this review. The present study is limited to a consideration of the use of the roentgen rays in the diagnosis, to the plans of treatment followed and, in so far as the information was available, to the late results of the injury.

To facilitate the study the patients are divided as follows:

Group 1. Patients seen prior to 1930
Group 2. Patients seen from 1930 to 1939 inclusive
Group 3. Patients seen from 1940 to 1951 inclusive

GROUP 1

A flat roentgenogram of the abdomen was made in five of the 9 cases comprising group 1. A retrograde pyelogram was done in 1 case. The records of the roentgenographic findings most frequently were limited to a notation of haziness of the area of the injured kidney, to a poor or no kidney shadow present and to variations in the size of the kidney or in definition of the psoas muscle shadow. One child was moribund when first seen; 2 children were considered too ill when admitted to the hospital to justify the delay necessary for roentgenological examination.

Five children in group 1 were treated by nonoperative measures. Two of these died a few hours after entering the hospital. One of the five returned 6 months after the injury because of persistent loin pain when a dilatation of the superior major calyx of the injured kidney was visualized on the retrograde pyelogram. There were no follow up notes in the records of the remaining two children treated by conservative measures.

Four of the patients in group 1 were operated on. A palpable mass in the loin was present on the injured side in each child. Nephrectomy was done on 2 patients. One was well and free of symptoms 1 year after operation. No follow-up notes were present in the record of one child whose kidney was removed; and no notes were found on the records of two children who had drainage of the perirenal space because of extravasated blood and urine.

GROUP 2

There were 15 children in group 2. Thirteen had excretory urograms made. These were diagnostic of the presence of the kidney injury in eleven but not of the degree of the kidney damage in seven children. Subsequently retrograde pyelograms were made in six of these 7 children, and were diagnostic of the degree of renal damage in each patient.

A conservative plan of treatment was followed in nine of the 15 children in group 2. Two died soon after admission to the hospital. The immediate recovery

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of the remaining 7 patients thus treated was stated to be satisfactory. However one child with no visualization of the superior major calyx on the excretory urogram, when first examined, had a normal pyelogram when dismissed from the hospital. Nevertheless 2 years later the patient had discomfort over the injured kidney region and the excretory urogram visualized progressive dilatation of the superior major calyx. One child with failure of visualization of the superior and middle calyces of an injured kidney, but with no mass in the loin, was reported well and free of symptoms 3 years after the accident. One boy treated conservatively had perirenal extravasation and a palpable mass in the loin when first seen. Operation was advised but refused. He was treated conservatively and was dismissed from the hospital a few weeks later free of symptoms and with no palpable mass present. Further urographic studies were not permitted and there were no follow up notes on the chart. There were no follow-up notes in the records of the other children in this group who were treated without operation.

Six of the children in group 2 were operated on. Each child had a palpable mass present. One child had normal pyelograms. She was first treated by conservative measures although a large tumor mass was present in the loin. The mass persisted and an exploratory laparotomy disclosed a perirenal hematoma present. This was not drained. There were no follow-up notes in this record. Drainage of perirenal extravasation was done in one boy who was reported well and free of symptoms 15 years after the accident. One child had an injury of congenital hydronephrosis and nephrostomy was done. The patient did not return subsequently for nephrectomy as advised and there were no follow up notes on the chart. Three patients of group 2 had a nephrectomy. All of these remained well and free of symptoms after dismissal from the hospital. One child whose kidney was removed had complete fracture of the kidney; one had hydronephrosis and a nephrocolonic fistula; and one had infected hydronephrosis. The last child had a kidney injury and a conservative plan of treatment was followed. The patient made a good recovery. Three years later the same kidney was again injured. At this time there was no visualization of the pelvis of the injured kidney on the excretory urogram. The immediate convalescence was prolonged and 4 months after the second accident a retrograde pyelogram disdisclosed an infected hydronephrotic sac which had developed following the first injury.

GROUP 3

There were 21 children in group 3. In 18, excretory urograms were diagnostic of the presence of the injury in fourteen, but failed to indicate the degree of the damage to the kidney in seven. Retrograde pyelograms were made in these 7 cases demonstrated the degree of kidney damage. Retrograde pyelograms were made in the follow up studies of three children. One of these made one year after the injury demonstrated increasing dilatation of the pelvis; in another case, progressive atrophy of the kidney was shown.

A conservative plan of treatment was followed in fourteen of the children in group 3. One child with injury of the kidney also had a rupture of the liver and died a few hours after first seen.

Three children who were not operated on had a palpable mass. One had extravasation of the injected medium throughout the kidney parenchyma. This child made a good immediate recovery, but atrophy of the kidney has developed and nephrectomy has been recommended. The children with a mass but no evidence of extravasation were reported well and free of symptoms 4 months, 1 year, and 5 years after the accident. One child who had no mass and who was treated conservatively returned 5 years after the accident because of discomfort on the injured side. Excretory and retrograde pyelograms were normal and no cause for the discomfort was found. One child in this group is now dying of urosepsis.

Seven children in group 3 were operated on. A nephrectomy was done in 5. Each patient who was operated on had a palpable mass, except one (fig. 1). No symptoms developed after dismissal from the hospital in any patient whose kidney was removed. They were reported well in the follow-up notes, 2½ months, 3 months, several months, 7 years, and 9 years after the operation. No follow-up notes were recorded on one child upon whom a nephrostomy had been done, and one with drainage of the perirenal space.

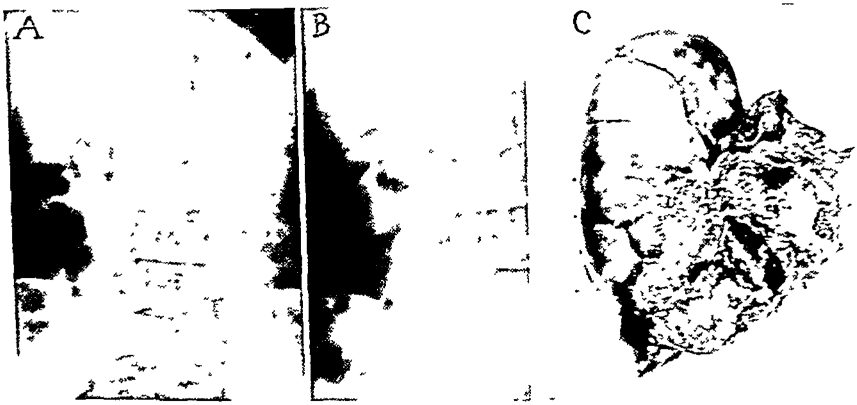

FIG. 1. *A*, L. L. No. 1577. Female 8 years old. Excretory urogram made November 25, 1950. Subcapsular extravasation. First seen 8 days after injury. Patient was comfortable, microscopic hematuria was present and no local tenderness or palpable mass was present in the loin. Patient treated by conservative measures for 2 weeks. *B*, excretory urogram made December 5, 1950, visualizing less concentration of extravasated dye, but showing increased dilatation of calyces. December 7, 1950, right lumbar nephrectomy. *C*, photograph of right kidney showing extent of extravasation. Ureter was obstructed at ureteropelvic juncture.

DISCUSSION

The roentgenographic examination of the children seen prior to 1930 was of little value in making a diagnosis of presence of a kidney injury and gave little or no indication of the severity of the kidney damage. Retrograde pyelography was not employed, although available at this time, except in the follow-up studies on one child. Instrumental difficulties in making a retrograde pyelogram and the irritating properties of the pyelographic medium available probably were most responsible for this omission.

When excretory urography became available in 1930, its value as an aid in making a diagnosis of an injury to the kidney was immediately recognized.

That the procedure had a special field of usefulness in the presence of this type of accident in a child was appreciated more and more as experience increased. Its discovery eliminated the need for transvesical instrumentation or surgical exploration in making a diagnosis of the presence of a kidney injury in most instances.

Excretory urography was used in thirty-one or 86 per cent of the 36 children with injury of the kidney seen since 1930. It was omitted in the study of 2 children who died soon after admission to the hospital; in 1 child who had a surgical injury of a hydronephrosis; in a patient seen in May 1930; and in one instance when the dressings for fracture of the ribs would have prevented sufficient detail for the pyelogram to have been diagnostic.

Excretory urography was considered diagnostic of the presence of a kidney injury in twenty-five of the 31 children in whom it was used. It failed to visualize sufficient evidences of the injury to warrant a diagnosis in 4 children. In 1 child a pelvic deformity on the excretory urogram was interpreted as due to a kidney injury. Exploratory operation disclosed a Wilms' tumor present. One child was given hippuran orally and there was no visualization of either kidney or pelvis.

The excretory urogram did not give reliable evidence of the degree of damage to the kidney in 13 children. Retrograde pyelograms were later made in each of these children, when sufficient evidence of the extent of the injury was obtained to complete the diagnosis. Also when the findings furnished by excretory urography in the follow up studies were uncertain, a retrograde pyelogram was made. Retrograde pyelography, without first an excretory urogram having being made, was done in only 1 case.

Twenty-eight of the 45 children were treated by nonoperative measures. Five of these died a few hours after admission to the hospital. The remaining 23 patients treated conservatively made good immediate recoveries. Omitting those children who died, satisfactory follow up notes are available in 11 records. Six of the children were reported well and free of symptoms. In three records it was noted that the children had a persisting loin pain or discomfort. Two of these had dilatation of a calyx presumably a result of the injury. The cause of the pain in the third child was not found although excretory and retrograde urographic studies were made. In 1 case uro-sepsis had developed. This patient had a spinal cord injury at the time of the accident and has resultant neurogenic bladder dysfunction. The record of one child treated conservatively states that atrophy of this kidney has since developed; nephrectomy has been recommended. There were no follow up notes in 12 patients treated by conservative measures.

Seventeen of the children were operated on. The immediate recovery was good in each patient. Follow-up notes were present in the records of but ten of these children. Each was reported to be well one year or more after the accident.

The records of 2 children stated they were emergency problems when admitted to the hospital and that immediate operation was necessary. Each of these children had a mass in the loin and severe loin pain. One was seen a few hours following the accident and had clinical evidences of intraperitoneal bleeding.

Twenty-four hours later an exploratory laparotomy disclosed a tear in the peritoneum overlying the injured kidney with blood passing from the perirenal space into the peritoneal cavity (fig. 2). The kidney was completely fractured

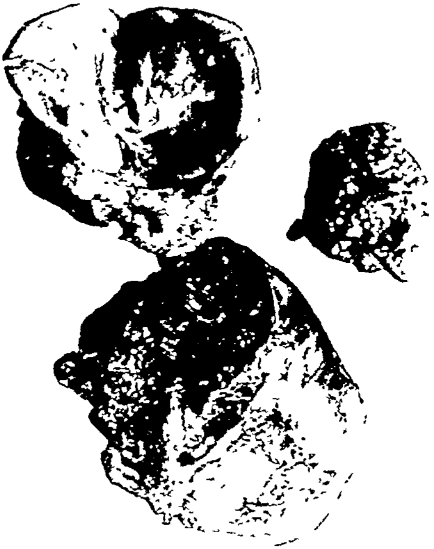

FIG. 2. L. L. No. 372. Male child 9 years old. Entered hospital January 14, 1929 a few hours after accident. Patient was in shock, had severe upper right quadrant pain, hematuria and mass in right loin. Evidences of intrapeiitoneal hemorrhage developed, and on January 15, 1929 exploratory laporatomy disclosed a tear in peritoneum overlying injured kidney. Peritoneal rent was closed and fractured kidney removed through lumbar incision.

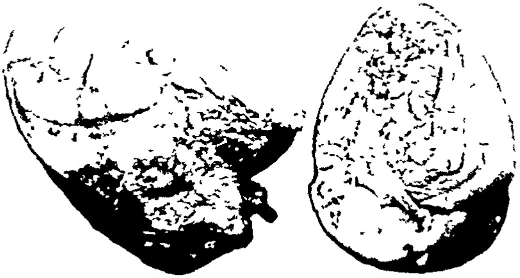

FIG. 3. J. G. No. 318. Male child 13 years of age. Patient was injured on June 23, 1929 and first seen July 16, 1929. Entered with mass in right loin and hematuria. Right lumbar nephrectomy with evacuation of three pints of fluid on July 17, 1929.

and the pieces were removed. The second patient had been injured 3 weeks before seen. An exploratory incision was made a few hours after hospital admission (fig. 3). The kidney had been completely fractured and the ureter was severed from the kidney. The pieces of kidney were removed. In addition, a third child was injured 10 days before seen. When admitted she was bleeding profusely, there was a large mass in the loin and the loin pain was severe and an immediate operation was advised. A few hours after admission to the hospital, a diagnosis of scarlet fever was made when she was placed on the isolation ward and the operation was postponed. Two weeks later, or 24 days after the accident, lumbar nephrectomy was done when two pieces of a completely fractured kidney were removed (fig. 4). In retrospect only the first child had a true emergency problem, not because of the injury to the kidney, but the associated tear in the peritoneum.

See figures 1, 2, 3, 4.

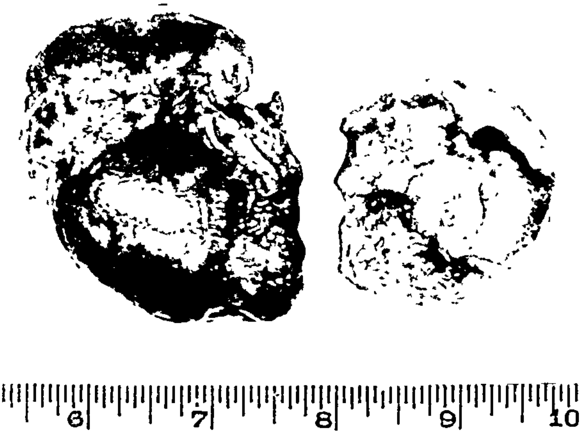

FIG. 4. S. M. No. 342. Girl 7 years old entered hospital May 18, 1930, ten days following injury to right kidney. She had severe upper right quadrant pain, profuse bleeding with clots in bladder, and palpable mass in right loin. Patient had scarlet fever when admitted. On June 1, 1930, through right loin incision, large amount of fluid was evacuated and completely fractured kidney was removed.

CONCLUSIONS

Roentgenographic findings in patients seen prior to 1930 were of limited value in diagnosing kidney injury in these patients.

Excretory urography was employed in nearly all children with a kidney injury seen since 1930.

Excretory urography proved a valuable aid in making a *diagnosis* of kidney injury.

Excretory urography not infrequently failed to give satisfactory evidence of the *degree of kidney damage* present.

Retrograde pyelography was employed as a follow up examination first when the excretory urogram failed to diagnose the presence of the injury, and second, when the degree of damage to the kidney was not visualized on the excretory urogram.

Retrograde pyelography was employed with an increasing frequency in the follow-up studies.

Twenty-eight children were treated by conservative measures and seventeen were operated on.

Excepting those children who died a few hours following the accident, each patient treated conservatively had a satisfactory immediate recovery.

The follow up notes of 5 children treated conservatively stated each subsequently developed symptoms the result of the injury. These were associated with pelvic dilatation in three, atrophy of the kidney in one and in one the cause of the discomfort over the previously injured kidney was not found. The injury was to a normal kidney in three of these 5 children.

The number of patients treated conservatively with adequate follow-up notes in the records, were insufficient to justify an opinion as to the frequency of a post traumatic complication. Hence this study warrants no conclusion as to the advisability of more radical treatment of this group of patients.

Most children who had a palpable mass, with or without extravasation of the pyelographic medium, were operated on.

Injury of the kidney in children, even though it be completely fractured, seldom in itself will demand an immediate surgical operation.

Associated injury of an intra-abdominal viscus, which possibility is always present in kidney injury, demands surgical operation so soon as diagnosed.

Nine of the 10 patients who had a nephrectomy were reported well and free of symptoms following the operation.

The records indicated the immediate prognosis in injury of the kidney in children irrespective of method of treatment is good.

There were no surgical deaths.

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UPPER URINARY TRACT DISEASE WITH SYMPTOMS SIMULATING HERNIATED NUCLEUS PULPOSUS

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Pain, resulting from upper urinary tract disease, and radiating to various areas of the human body, has been the topic of many medical reports. Because of the atypical manifestations the differential diagnosis has been difficult and not infrequently the causative lesion has been overlooked. Lowsley and Twinem in 1929 discussed a series of 84 patients with urinary tract disease who had been referred to the urological service, having been treated for some other condition without obtaining relief. In this series, 47.5 per cent had been subjected to surgery other than urologic. The most frequent type of surgery performed was appendectomy.

The literature contains many individual case reports of urinary tract lesions with symptoms simulating pleurisy, peptic ulcer, intestinal obstructions, diverticulitis, hepatitis, gallbadder disease, retroperitoneal tumors, and diseases of the female adnexa. Pain may also radiate to the lower extremities and the severe incapacitating sciatic pain from extensive pelvic metastases of prostatic carcinoma is well known.

Ockerblad and Carlson presented an interesting summary of referred pain from the urinary tract. By stimulating the renal pelvis and various levels of the ureter with an electrode tipped ureteral catheter, they were able to demonstrate pain starting at the flank, radiating anteriorly to the lower abdominal wall and at times descending down the leg to the foot.

Grellet, in the Paris Medical Bulletin, discussed the presence of sciatic pain co-existing in patients with calculi of the upper urinary tract. It was his opinion that they were not separate entities but that the former was referred pain from motion or position of the calculi. Haines has published a case report of a ureteral calculus producing sciatic pain, the symptoms of which disappeared following ureterolithotomy.

Since Mixter and Barr described the surgical treatment of ruptured intervertebral disc in 1934, sciatic pain has been closely interrelated with that diagnosis. Radiating pain to the lower extremity has frequently been diagnosed as herniated nucleus pulposus although surgical intervention has not always brought relief of symptoms. Montero reported a case of sciatic pain due to polycystic renal disease and stated that sciatica is rarely mentioned as a painful symptom of renal tumors.

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Femoral nerve pain may be mistaken for sciatic type pain. Pow reported a case of retroperitoneal sarcoma involving the iliopsoas muscle and infiltrating the nerves extending down to Poupart's ligaments. He probably referred to the femoral nerve which is in close anatomical association with the iliopsoas muscle and does descend under Poupart's ligament. The pain in this case radiated to the lateral and anterior aspects of the thigh. Shewket described a case of concomitant symptoms of acute appendicitis and radiating pain to the right hip, leg and toes. The pain was incapacitating. The patient was treated conservatively and 6 months later an exploratory laparotomy revealed the appendix firmly adherent to the femoral nerve. The trauma caused by separating the appendix from the femoral nerve produced similar symptoms of radiating leg pain which subsided after one week.

Pain sensation arising from renal and ureteral lesions is known as visceral pain. The location of the terminal nerve endings in the kidney and ureter have not been definitely determined. Whether the sensory nerve cells end in the mucosa, muscular wall, adventitia, or in the adjacent surrounding structures as peritoneum is still a matter of discussion and many conflicting theories have been reported. However, the sensory stimuli are conducted through the splanchnic nerves passing through the celiac ganglion to the sympathetic ganglia segments of D-11 to L-2. Thence they proceed through the posterior roots to the spinal cord.

Ray, Neil and others have experimentally produced pain by electrical stimuli, by pressure and distention of the renal pelvis and ureter. Ray and Neil have shown that electrical stimulation of the renal capsule did not provoke any painful response, but that the typical renal pain manifested by referred pain to the flank and lower abdominal wall was elicited when pressure or stretching was applied to the renal pedicle. They noted that the painful stimuli from the kidney and ureter were eliminated after the sympathetic ganglia segments from D-11 to L-1 were excised. Lewis, White, Smithwick, and others believe that the L-2 segment also carries impulses from the upper urinary tract.

The efferent impulses to the spinal cord are conducted along the sympathetics but the afferent pain response is experienced through parasympathetic nerves located at the same segmental levels. Thus flank pain, lower abdominal and groin pain represent the skin dermatomes from D-11 to L-2. This is a result of the transfer of visceral stimuli to the somatic neurons. Various opinions have been offered regarding the method of this procedure. Ross suggested that the visceral sensory stimuli entering the spinal cord diffused to the neighboring somatic nerves in the same segment. Pottenger considered the visceral stimuli to lower the pain threshold of the somatic nerves in the same segment. Lewis is of the opinion that there are definite visceral sensory tracts extending to the brain but that the localization of these impulses in the brain are imperfect, resulting in a response through somatic nerves leaving the cord at the same segmental level (fig. 1).

The femoral nerve arises from the spinal segments L-2 to L-4. This would indicate that in addition to the typical flank and abdominal pain, lower extremity pain would be a frequent clinical symptom in lesion of the upper urinary tract.

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Pain, resulting from upper urinary tract disease, and radiating to various areas of the human body, has been the topic of many medical reports. Because of the atypical manifestations the differential diagnosis has been difficult and not infrequently the causative lesion has been overlooked. Lowsley and Twinem in 1929 discussed a series of 84 patients with urinary tract disease who had been referred to the urological service, having been treated for some other condition without obtaining relief. In this series, 47.5 per cent had been subjected to surgery other than urologic. The most frequent type of surgery performed was appendectomy.

The literature contains many individual case reports of urinary tract lesions with symptoms simulating pleurisy, peptic ulcer, intestinal obstructions, diverticulitis, hepatitis, gallbadder disease, retroperitoneal tumors, and diseases of the female adnexa. Pain may also radiate to the lower extremities and the severe incapacitating sciatic pain from extensive pelvic metastases of prostatic carcinoma is well known.

Ockerblad and Carlson presented an interesting summary of referred pain from the urinary tract. By stimulating the renal pelvis and various levels of the ureter with an electrode tipped ureteral catheter, they were able to demonstrate pain starting at the flank, radiating anteriorly to the lower abdominal wall and at times descending down the leg to the foot.

Grellet, in the Paris Medical Bulletin, discussed the presence of sciatic pain co-existing in patients with calculi of the upper urinary tract. It was his opinion that they were not separate entities but that the former was referred pain from motion or position of the calculi. Haines has published a case report of a ureteral calculus producing sciatic pain, the symptoms of which disappeared following ureterolithotomy.

Since Mixter and Barr described the surgical treatment of ruptured intervertebral disc in 1934, sciatic pain has been closely interrelated with that diagnosis. Radiating pain to the lower extremity has frequently been diagnosed as herniated nucleus pulposus although surgical intervention has not always brought relief of symptoms. Montero reported a case of sciatic pain due to polycystic renal disease and stated that sciatica is rarely mentioned as a painful symptom of renal tumors.

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Read at annual meeting, Mid-Atlantic Section American Urological Association, Old Point Comfort, Va., April 14, 1951.

The spine was inclined forward and to the right. The lungs were normal; the heart was enlarged. The blood pressure was 200/115. In the left upper quadrant of the abdomen a large nontender, movable, firm, smooth mass was palpated. The mass extended from beneath the costal margin to the umbilicus. Mesially the mass reached the midline. The prostate was enlarged, slightly tender, firm and nodular. The left leg was carried in a flexed position and any passive movement to straighten the leg was painful. There was no evidence of atrophy of the left leg. A diagnosis of a possible left renal tumor and herniated nucleus pulposus was considered.

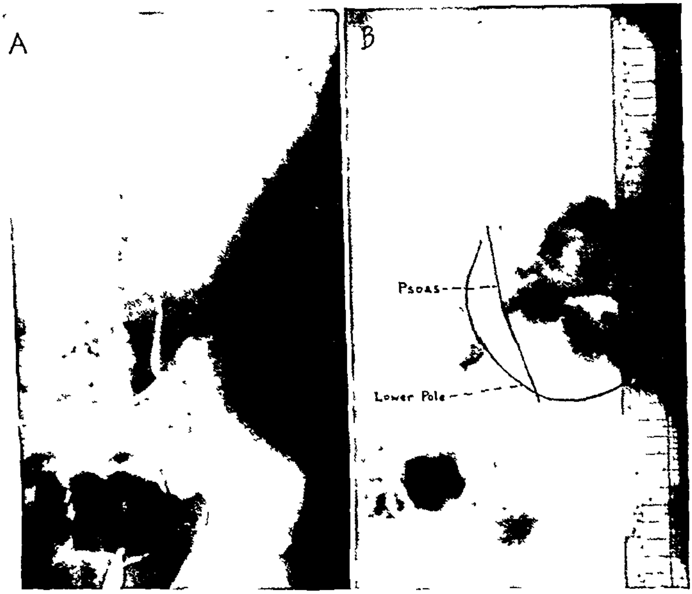

FIG. 2. Case 1. *A*, retrograde pyelogram reveals distorted calyces of left kidney. *B*, diagrammatic outline of lower pole of left kidney and its relation to psoas muslce.

The laboratory reports were normal. The plain urogram visualized a large mass obscuring the left midabdomen. The excretory urogram demonstrated excretion of the opaque dye in the right kidney but no contrast medium was seen on the left side. X-rays of the left shoulder revealed several hypertrophic excrescences over the upper border of the acromion. On cystoscopy a grade 2 prostatic hyperplasia of the lateral lobes was seen. A left retrograde pyelogram (fig. 2, *A*) showed the upper and middle calyces to be displaced medially. A preoperative diagnosis of malignancy was made and a left nephrectomy was performed on October 5, 1949. During the operation the lower pole was inadvertently ruptured causing about 300 cc of chocolate brown hemorrhagic fluid to escape. Figure 2, *B* is a diagrammatic outline of the lower pole of the left kidney showing its relation to the psoas muscle. Postoperative convalescence was uneventful, except that when ambulant, the patient remarked about the complete absence of the left hip and leg pain. He no longer carried his left leg in flexion and was able to walk without a limp.

The latter, however, has been an infrequent symptom, and therefore, the cause of the referred extremity pain has been looked for elsewhere. It is believed that in certain lesions of the upper urinary tract, radiating pain to the lower extremities may be due to direct stimulation of the femoral and sciatic nerves. This may occur by pressure on the adjacent nerves or by direct continuity of an inflammatory process to the neighboring nerve.

Three cases of upper urinary tract disease have been encountered with the predominating symptom of referred pain to the lower extremities. Two of these cases were admitted directly to the neurosurgical service with a diagnosis of herniated nucleus pulposus and that diagnosis was under consideration in a third case admitted directly to the urological service. Two of these cases had renal disease; namely, polycystic renal disease and unilateral multilocular cysts with hemorrhage. The third case was one of an impacted calculus that did not present any clinical symptoms of urinary tract disease. These patients on admission demonstrated the typical inclined posture of the trunk and flexion of the involved leg. The gait was limping and the body weight shifted to the other leg.

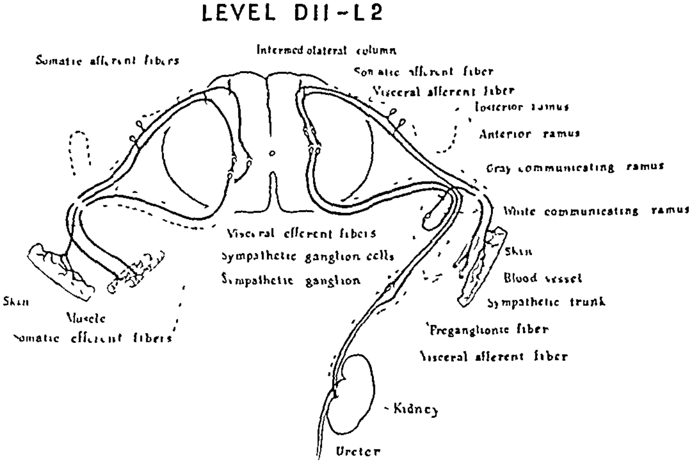

FIG. 1. Diagrammatic outline of visceral and somatic nerve routes at D-11—L-2 levels. (Adapted from Kuntz.)

CASE REPORTS

Case 1. T. L. D., Reg. No. 11 096, a 62 year old white man, was admitted to the hospital on September 21, 1949, complaining of severe pain in the left hip and shoulder for several weeks. In addition he complained of frequency, nocturia four to five times, hesitancy and a weak dribbling urinary stream. He complained of severe pain over the left hip radiating down the leg to his ankle. The pain was incapacitating and he had been unable to work for several weeks. Left shoulder pain was also present, especially on motion. He denied any history of a traumatic injury to his back. His appetite was good but he admitted a weight loss of 70 pounds in 2 years.

Physical examination disclosed a well developed, well nourished, white man walking with a limp protecting the left leg which was kept in a flexed position.

and he was able to walk upright without limping. He has been followed to date, and denies recurrence of the sciatica of the left leg.

Case 3. H. M. S., Reg. No. 18 398, a 64 year old white man, was admitted to the neurosurgical service on January 20, 1949, complaining of low back pain which radiated down the right leg. The pain had been present since February 1919, when he suffered his first sudden onset of severe pain in his back radiating down the right hip and leg. He was able to get around with difficulty and developed a limping gait. A diagnosis of sciatica was made at that time. The pain gradually subsided but since then this same type of pain had recurred every one–two years. The duration of each episode lasted about two days to three weeks. The back and leg pain became more pronounced in 1947–48. About two months ago, the patient had a check-up at a local hospital where a diagnosis of a herniated nucleus pulposus was made. Physical examination on admission revealed normal heart and lungs. The blood pressure was 120/70. Examination of the back disclosed tenderness at L-4 and to the right of L-4 interspace. Bending to the left was limited, but not to the right. No erector muscle spasm or scoliosis was noted. The neurological examination was negative. A diagnosis was made of sciatica due to residuals of an old H.N.P. with adhesions about the L-4 nerve root. The laboratory work-up was normal. The spinal fluid and the gold curve negative for any luetic involvement.

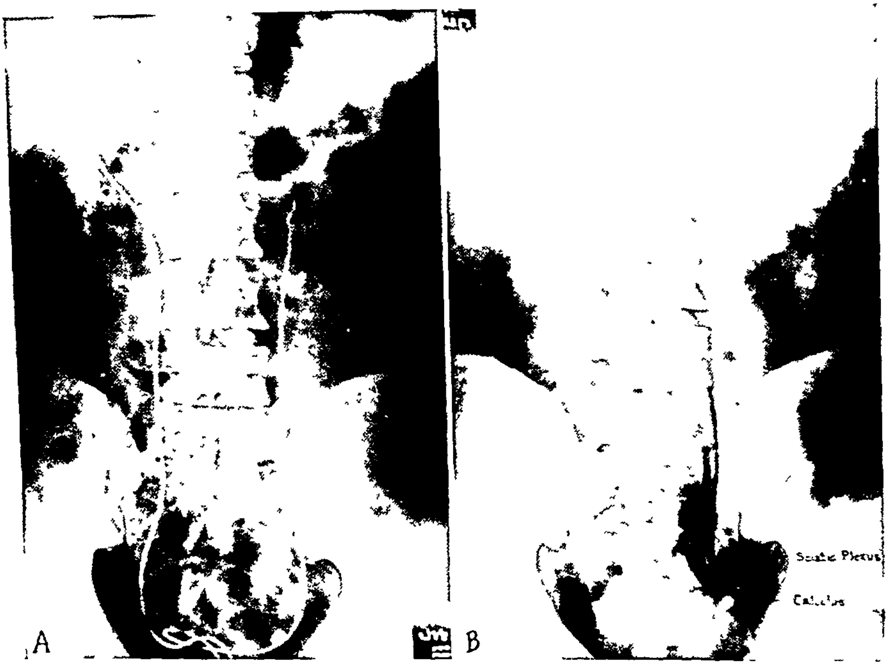

FIG. 3. Case 2. *A*, retrograde pyelogram with indwelling ureteral catheters. Note large calculus in lower third of left ureter. *B*, diagrammatic outline showing relation of calculus to sciatic plexus.

The x-ray of the spine showed a slight narrowing of the L-5 interspace, and

Gross examination of the removed kidney, which measured 19 cm. by 10 cm. by 11 cm., revealed three large cystic compartments containing reddish brown friable material. No evidence of any malignancy was found. A diagnosis of multilocular cysts with hemorrhage of the left kidney was made.

The patient has been under observation since his discharge and denies any recurrence of the left sciatic pain.

Case 2. J. L. C., Reg. No. 14 686, a 37 year old white man, was admitted February 25, 1948 complaining of low back pain radiating downward to his left hip and leg since 1945. At that time he suffered a back injury when he fell from a boom for a distance of 20 feet, and landed on another man. No evidence of fracture of the spine was found and he was hospitalized 5 weeks, being placed on bed boards. In addition he was told he bruised his kidney and had purulent urine. He denied hematuria. He improved and did well until December 1947, when severe low back pain developed radiating down to his left leg. Since then he had been more or less bedridden. The pain was aggravated by coughing, sneezing and straining. He was treated by his local physician for sciatica and finally referred to the neurosurgical service with a diagnosis of herniated nucleus pulposus.

Physical examination showed a man who appeared older than his stated age, standing with a marked forward tilt of the pelvis and entire spine. Heart and lungs were normal. The blood pressure was 126/80. The patient favored his left leg and a reversal of the normal lordosis was present with associated spasm of the left paravertebral muscles in the lumbar region. Motion of the lumbosacral spine was limited approximately 90 per cent. Pressure over the left intervertebral space of L-5 caused severe radiating pain to the left hip and knee. There was no significant atrophy, muscle weakness, or sensory loss in either extremity. A probable diagnosis of H.N.P. at the level of L-5 intervertebral space on the left side was considered.

The laboratory findings were normal except for 6–8 white blood cells per high powered field in the urine. The x-rays of the lumbar spine showed a complete loss of the lordotic curve, but no diminution in the diameter of the interspaces.

On March 1 a lumbar puncture was performed. Intraspinal pressure and dynamics were normal. A myelogram was made at the same time but a definite diagnosis of a ruptured intervertebral disc could not be made on the basis of the x-rays. The patient was transferred to the urological service, where the x-rays indicated calcific densities over both kidneys and in the left half of the bony pelvis. Plain and excretory urograms revealed a calculus in the inferior calyx of the right renal pelvis, one in the upper third of the right ureter and one in the lower third of the left ureter just above the ischial spine. Gravel was also visualized in the lower pole of the left kidney.

Retrograde pyelograms were made (fig. 3) and the left ureteral calculus was bypassed with some difficulty, being dislodged from its impacted position. On the following day the left sciatic pain had completely disappeared. The ureteral calculus was passed spontaneously following the removal of the left ureteral catheter which had remained indwelling for 4 days. The right ureteral and renal calculi were removed surgically. The pain in the left hip and leg did not recur, and he was able to walk upright without limping. He has been followed to date, and denies recurrence of the sciatica of the left leg.

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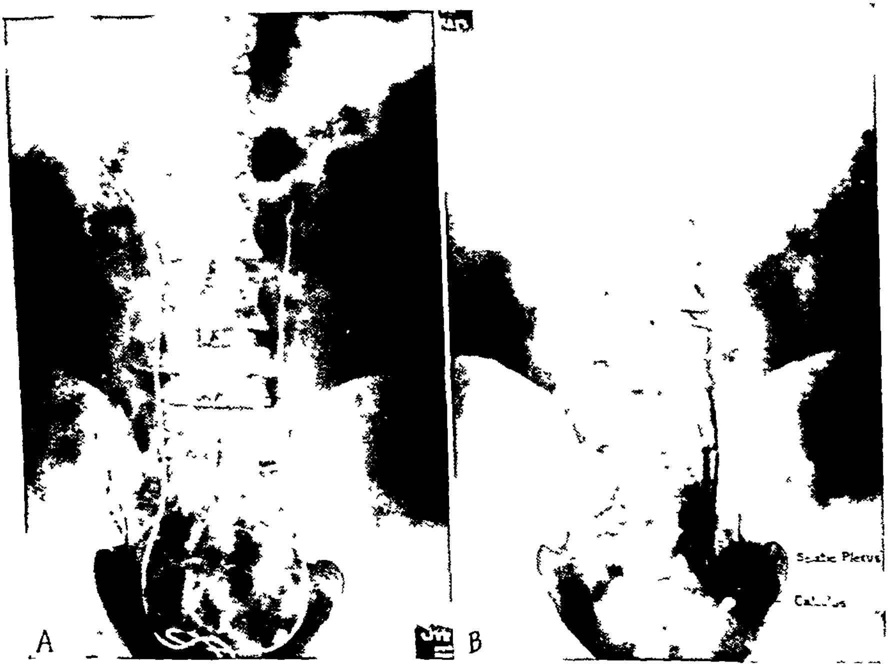

FIG. 3. Case 2. *A*, retrograde pyelogram with indwelling ureteral catheters. Note large calculus in lower third of left ureter. *B*, diagrammatic outline showing relation of calculus to sciatic plexus.

The x-ray of the spine showed a slight narrowing of the L-5 interspace, and osteoporosis of L-5. The x-ray also indicated the presence of enlarged renal shadows bilaterally. The patient was referred to the urological service.

On January 26, 1949 an excretory urogram revealed enlarged renal shadows with poor visualization of the calyceal system which appeared elongated. On January 31, retrograde studies were made. Renal function was essentially normal with indigo carmine dye reappearing from the catheters 3 minutes after the intravenous injection and with 4 plus concentration. The x-rays demonstrated elongated major and minor calyces (fig. 4). The right ureter was moderately deviated toward the midline in the region of the right sacroiliac joint. A diagnosis of polycystic renal disease was made.

In view of the patient's age and good renal function with the absence of severe sciatic symptoms, surgical intervention was deferred. The patient has been followed to date and has presented no recurrence of these symptoms.

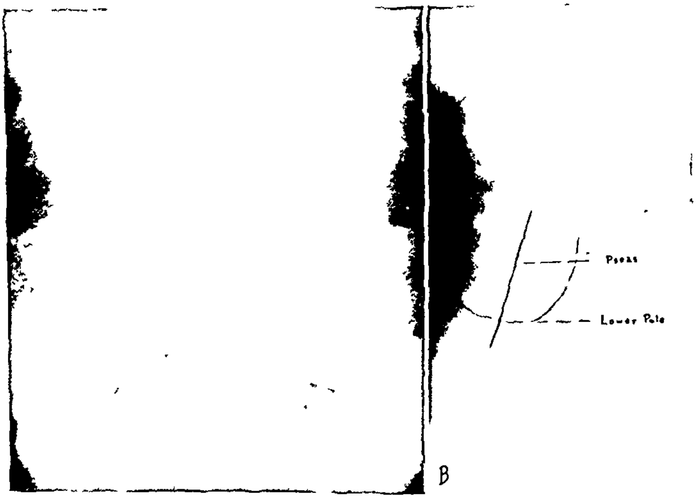

FIG. 4. Case 3. *A*, retrograde pyelogram outlines calyceal system typical of large polycystic kidneys. *B*, diagrammatic outline of lower pole of right kidney and its relationship to psoas muscle. Upright film reveals mobility of this kidney (compare with *A*).

COMMENT

For better comprehension of the possible cause of this type of referred pain, a topographical examination was made at five autopsies. The anatomical relationships between the kidney and ureters to the nerves and muscles that might be involved in transmitting pain to the extremities were studied. It was noted that the femoral nerve arising from L-2–L-4 emerged from behind the psoas muscle into the retroperitoneal cavity at a level corresponding to the lower half of the fifth lumbar vertebral body. The distance between this point and the dome of the diaphragm averaged 22–24 cm. Thus, a markedly enlarged kidney could be expected to rest on this nerve and produce pressure symptoms of pain to the involved extremity. The iliac muscle in this area extends ventrally and caudally and could act as a supporting base for an enlarged kidney, thus localizing the renal weight and increasing the possibility of marked pressure on the nerves at that point.

Case 2 illustrates complete absence of typical symptoms of the presence or movement of ureteral calculi. The x-ray revealed the localization of the calculus about 4 cm. above the left ureterovesical junction. There is no way of determining how long the calculus was impacted in that area, especially since urinary drainage from the renal pelvis was not obstructed.

Anatomical studies of the bony pelvis revealed that the ureter crosses the sacral plexus anteriorly, superior to the larger sciatic foramen. The plexus is separated from the ureter by the endopelvic fascia. It is conceivable that periureteritis could, by direct extension of the local inflammatory reaction, involve the perineural sheath, or that constant pressure could be exerted on the sciatic nerve by the impacted calculus. With the history of a back injury, radiating sciatic pain and absence of urinary symptoms, a diagnosis of a herniated intervertebral disc could thus very easily be considered.

Although the third case was not subjected to surgery, the diagnostic impression is that the enlarged polycystic kidney on the right side caused the radiating pain down the right leg as a result of pressure on the femoral nerve. The recurrent episodes of pain over a period of years may be explained by the formation of new cysts or enlargement of existing cysts. Rupture of cysts or position changes of the enlarged movable kidney could produce the remissions of his complaints. Although it is not a proven case, it was believed that it should be included in this series.

A visual explanation of the anatomical relationships in the three cases was attempted by superimposing a rough sketch of the involved structures on the x-ray films.

SUMMARY

Three cases of upper urinary tract disease have been presented with predominant symptoms of radiating lower extremity pain simulating ruptured intervertebral disc. The patients had no symptoms of upper urinary tract disease.

It is the opinion of the authors that referred pain to the lower extremities may occur if direct stimulation of the femoral or sciatic nerve results from disease of the upper urinary tract. This stimulation may be caused by direct continuity of an inflammatory lesion or by direct pressure on the nerves.

It is hoped that sciatic pain will be recognized as a symptom of possible upper urinary tract disease, and that a urological evaluation be considered in the differential diagnosis of radiating pain to the lower extremities.

Veterans Administration Hospital, East Orange, New Jersey (*M. M.*)

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MODERN TREATMENT OF ACUTE RENAL FAILURE

SAMUEL A. VEST AND ROBERT A. KELLEY

From the Department of Urology, University of Virginia Hospital, Charlottesville, Va.

The principles involved in the treatment of acute or total renal failure should be of considerable concern to the urologist. Anuria usually results in a state of therapeutic desperation and despair in which a wide variety of treatment is frantically applied. For this reason, it may be worthwhile periodically to review the basic principles of this problem.

Uremia, in general, has long been thought to be a syndrome resulting mainly from the retention of waste products of nitrogen metabolism, but it is far more complex than the failure to excrete any single nitrogenous substance. Modern knowledge clearly indicates that the most important disturbance in renal insufficiency is the failure of the kidney to maintain a proper volume of body fluid and the chemical equilibrium of various electrolytes within the plasma and other fluid compartments of the body. Disturbance in fluid and electrolyte balances account for most uremic symptoms, especially those of the central nervous system. Proper maintenance of fluid and electrolyte balance is, therefore, the cardinal therapeutic objective.

We are all aware of the great strides made by our specialty over the last several decades in the development of instruments for the relief of obstructions. There are other fields in which we, as urologists, should be just as proficient. They include renal physiology and subjects that concern water, electrolyte, and protein balances. It is only by an understanding of such basic processes that we are able to properly interpret the abnormal and to plot a sound therapeutic course in our urological patients. We, as urologists of today, must not allow ourselves to become pure mechanicians but must assume personal responsibility for the clinical application of the advancements in the various biochemical and physiological processes which are concerned with kidney function in our patients.

This discussion is not concerned with the correction of obstructions to the urinary tract, such as calculi, tumors, etc., which could produce anuria. It is intended only to consider acute failure of the anuric and oliguric type as a result of either prerenal or intrarenal disorders. So-called "prerenal conditions," such as shock associated with reduced renal blood flow and its attendant anoxia, dehydration of various types, electrolyte imbalance, such as hypochloremia, etc., may result in temporary loss of renal function, which if allowed to persist lead to anatomical or intrinsic renal lesions with anuria.

You are also familiar with the other and more common etiologic factors (now some 40-odd) encountered in the production of intrinsic renal lesions and especially with those conditions associated with pigment excretion. The latter includes mismatched transfusions, crushing muscle injuries, hemorrhage, and hemolysis following transurethral resections. Various toxins and poisonous substances are also often implicated.

Read at annual meeting, South Central Section, American Urological Association, Tulsa, Okla., September 16, 1950.

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You are also familiar with the other and more common etiologic factors (now some 40-odd) encountered in the production of intrinsic renal lesions and especially with those conditions associated with pigment excretion. The latter includes mismatched transfusions, crushing muscle injuries, hemorrhage, and hemolysis following transurethral resections. Various toxins and poisonous substances are also often implicated.

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We are not concerned primarily with a review of the exact pathology of the renal lesion in anuria. The term "lower nephron nephrosis" has been most unfortunate, and pathologists now recognize that whatever the inciting cause, the process is more likely to involve the complete nephron and not specifically the distal tubule. Pathologically one encounters various degrees of damage to the cells of the entire tubule. The glomerular filtrate finds egress back into the venous system or peritubular veins through the injured cells and by tubulovenous anastomoses.

Therapy in the past has often been erroneously based on the supposition that anuria was due solely to the obstruction by casts, and treatment was directed to the immediate re-establishment of urine flow. Osmotic diuretics in the form of phosphates, sulfates, and various hypertonic sugars have been employed on the theory that they would increase pressure within the tubules and expel the casts. In spite of the now-accepted pathogenesis, therapy of anuria is frequently on an unsound basis. One author recently reviewed the 101 most recent cases treated in the literature and found a wide diversity of therapeutic procedures, including: renal decapsulation, forcing of fluids, restriction of fluids, intravenous procaine, sodium sulfate diuretics, spinal anesthesia, peri-arterial de-innervation, sympathetic block, as well as the use of alkalies and sympathetic paralyzing drugs. The most significant feature of anuria due to such "nephron" injuries (predominantly tubular) is that, given sufficient time, usually two to three weeks, the cells of the tubules will soon regenerate and resume function. With such reversible lesions the patient must be kept alive, and proper therapy becomes of paramount importance.

The majority of fatal anuric cases have died within the first week or ten days, thus indicating that causes other than the temporary absence of renal function are in effect. Dogs, properly managed, can be kept alive for 70 days or more following bilateral nephrectomy. From animal experiments, it is calculated that man should theoretically live 3 to 4 weeks without renal function. Stock observed one man to live 46 days, with the total excretion of approximately 1000 cc urine.

What, then, are the common causes of death in reversible renal injuries? The first is undoubtedly overhydration, and the second is disturbances in electrolytes, especially potassium and occasionally sodium. The other causes may be hormonal imbalances, an accumulation of unknown and known toxic metabolites, such as quanidine, phenols, paracresols, and organic acids.

What are the objectives in the treatment of total renal failure? They are mainly the prevention of any derangement of the internal electrolyte and fluid environment. Any imbalances that occur or may already have occurred when the patient is first seen must be cautiously corrected. A second objective is the control, as far as feasible, of metabolism. Other objectives are so-called supportive therapy and the possible removal of waste products and excess electrolytes by various artificial dialyses. The treatment of anuria requires extreme vigilance and is never a passive affair.

FLUID BALANCE

In anuria the first therapeutic consideration is fluid balance. With the suspension of kidney function, water will be lost only through the so-called insensible routes. For management, one must consider such losses in a rather precise manner. Under average temperature conditions there is a relentless water loss each 24 hours, calculated, in general, to be 0.5 to 0.6 cc per kilogram of body weight per hour. This daily insensible loss for the average man is about 1000 cc, proportioned roughly as 500 cc through the lungs, 300 to 400 cc through the skin, and 100 cc in the feces. Inasmuch as 200 cc of water is liberated each day by the body's metabolism, one may consider that a 70 kilo man will lose approximately 800 cc of water per day, and a total fluid intake of this amount is necessary for a proper fluid balance to exist. When environmental or seasonal temperatures are high, as well as when fever exists, this insensible loss may be doubled or tripled. With active perspiration, it must be appreciated that sometimes several liters of fluid may be lost. If diarrhea or vomiting occurs, this volume must be accurately measured and added to the daily insensible loss. In the case of oliguria, the urine volume must also be added to the above calculated intake.

In consideration of fluid appraisal the first procedure is a careful history of what has taken place up to the time the patient has been seen. An estimation of the amount of emesis is important, as is the amount of fluid the patient may have received by mouth or vein. This is followed by a clinical estimation of the volume of the extracellular compartments, i.e., the state of hydration. Unfortunately, tests to determine the volume of plasma have not been developed to a point where they are practical for use in anuric patients. Some basic idea of the state of hydration may be gained by the well-known physical signs, which include: degree of dryness or moisture of the mucous membranes, presence or absence of edema, texture of the skin and condition of the subcutaneous tissue, liver enlargement, fullness of the peri-orbital tissues, presence or absence of moisture in the lungs, venous pressure, as well as various tests concerning the collapsibility of the veins of the extremities in different postures. Frequent determinations of plasma proteins and hematocrit may also help to indicate the degree of hydration. One cannot rely upon the concentration of cations such as sodium as an index of the body fluid volume, as sodium values are more complex. One can categorically state that the plasma electrolyte concentrations are not always an index of total electrolyte content or total fluid volume in the extracellular spaces. An initial body weight is very important, because daily variations reflect changes in the total water content of the body and ultimately in the size of the internal fluid compartments. A sudden change in weight of 2 pounds indicates a variation in body water of one liter.

A proper clinical examination as outlined above should lead to a reasonable deduction as to the state of hydration. Dehydration, even with normal kidneys, is inimical to the resumption of normal kidney function and should be corrected. Overhydration may result in pulmonary edema or cardiac failure. The continu-

We are not concerned primarily with a review of the exact pathology of the renal lesion in anuria. The term "lower nephron nephrosis" has been most unfortunate, and pathologists now recognize that whatever the inciting cause, the process is more likely to involve the complete nephron and not specifically the distal tubule. Pathologically one encounters various degrees of damage to the cells of the entire tubule. The glomerular filtrate finds egress back into the venous system or peritubular veins through the injured cells and by tubulovenous anastomoses.

Therapy in the past has often been erroneously based on the supposition that anuria was due solely to the obstruction by casts, and treatment was directed to the immediate re-establishment of urine flow. Osmotic diuretics in the form of phosphates, sulfates, and various hypertonic sugars have been employed on the theory that they would increase pressure within the tubules and expel the casts. In spite of the now-accepted pathogenesis, therapy of anuria is frequently on an unsound basis. One author recently reviewed the 101 most recent cases treated in the literature and found a wide diversity of therapeutic procedures, including: renal decapsulation, forcing of fluids, restriction of fluids, intravenous procaine, sodium sulfate diuretics, spinal anesthesia, peri-arterial de-innervation, sympathetic block, as well as the use of alkalies and sympathetic paralyzing drugs. The most significant feature of anuria due to such "nephron" injuries (predominantly tubular) is that, given sufficient time, usually two to three weeks, the cells of the tubules will soon regenerate and resume function. With such reversible lesions the patient must be kept alive, and proper therapy becomes of paramount importance.

The majority of fatal anuric cases have died within the first week or ten days, thus indicating that causes other than the temporary absence of renal function are in effect. Dogs, properly managed, can be kept alive for 70 days or more following bilateral nephrectomy. From animal experiments, it is calculated that man should theoretically live 3 to 4 weeks without renal function. Stock observed one man to live 46 days, with the total excretion of approximately 1000 cc urine.

What, then, are the common causes of death in reversible renal injuries? The first is undoubtedly overhydration, and the second is disturbances in electrolytes, especially potassium and occasionally sodium. The other causes may be hormonal imbalances, an accumulation of unknown and known toxic metabolites, such as quanidine, phenols, paracresols, and organic acids.

What are the objectives in the treatment of total renal failure? They are mainly the prevention of any derangement of the internal electrolyte and fluid environment. Any imbalances that occur or may already have occurred when the patient is first seen must be cautiously corrected. A second objective is the control, as far as feasible, of metabolism. Other objectives are so-called supportive therapy and the possible removal of waste products and excess electrolytes by various artificial dialyses. The treatment of anuria requires extreme vigilance and is never a passive affair.

FLUID BALANCE

In anuria the first therapeutic consideration is fluid balance. With the suspension of kidney function, water will be lost only through the so-called insensible routes. For management, one must consider such losses in a rather precise manner. Under average temperature conditions there is a relentless water loss each 24 hours, calculated, in general, to be 0.5 to 0.6 cc per kilogram of body weight per hour. This daily insensible loss for the average man is about 1000 cc, proportioned roughly as 500 cc through the lungs, 300 to 400 cc through the skin, and 100 cc in the feces. Inasmuch as 200 cc of water is liberated each day by the body's metabolism, one may consider that a 70 kilo man will lose approximately 800 cc of water per day, and a total fluid intake of this amount is necessary for a proper fluid balance to exist. When environmental or seasonal temperatures are high, as well as when fever exists, this insensible loss may be doubled or tripled. With active perspiration, it must be appreciated that sometimes several liters of fluid may be lost. If diarrhea or vomiting occurs, this volume must be accurately measured and added to the daily insensible loss. In the case of oliguria, the urine volume must also be added to the above calculated intake.

In consideration of fluid appraisal the first procedure is a careful history of what has taken place up to the time the patient has been seen. An estimation of the amount of emesis is important, as is the amount of fluid the patient may have received by mouth or vein. This is followed by a clinical estimation of the volume of the extracellular compartments, i.e., the state of hydration. Unfortunately, tests to determine the volume of plasma have not been developed to a point where they are practical for use in anuric patients. Some basic idea of the state of hydration may be gained by the well-known physical signs, which include: degree of dryness or moisture of the mucous membranes, presence or absence of edema, texture of the skin and condition of the subcutaneous tissue, liver enlargement, fullness of the peri-orbital tissues, presence or absence of moisture in the lungs, venous pressure, as well as various tests concerning the collapsibility of the veins of the extremities in different postures. Frequent determinations of plasma proteins and hematocrit may also help to indicate the degree of hydration. One cannot rely upon the concentration of cations such as sodium as an index of the body fluid volume, as sodium values are more complex. One can categorically state that the plasma electrolyte concentrations are not always an index of total electrolyte content or total fluid volume in the extracellular spaces. An initial body weight is very important, because daily variations reflect changes in the total water content of the body and ultimately in the size of the internal fluid compartments. A sudden change in weight of 2 pounds indicates a variation in body water of one liter.

A proper clinical examination as outlined above should lead to a reasonable deduction as to the state of hydration. Dehydration, even with normal kidneys, is inimical to the resumption of normal kidney function and should be corrected. Overhydration may result in pulmonary edema or cardiac failure. The continuous and insensible water loss will in time reduce overhydration, but if there is impending pulmonary edema or heart failure, an emergency phlebotomy may be in order. Water can also be rapidly withdrawn from the internal fluid compartments by injection of a proper hypertonic solution into the peritoneal cavity or by the use of an artificial kidney.

ELECTROLYTES

In anuria the plasma electrolyte concentrations should be maintained as near normal as possible for proper cell functioning and prolongation of life. If the fluid (water) volume of the internal compartments is within approximately normal limits, then any deviations from the normal concentrations of plasma electrolytes are significant, and corrective procedures are in order. Sodium and potassium, as the main cations, and chloride, as the main anion, are of primary consideration. The role of magnesium, phosphates, and sulfates is not fully understood at the present time, but under no condition should they be allowed to find ingress into the plasma as a result of any therapeutic procedure. Diuretics containing such substances which cannot be excreted in anuria are contraindicated. Calcium and magnesium form such a small proportion of the total plasma electrolyte content that moderate deviations are probably not significant. As a result of phosphate retention, the plasma calcium concentration may fall to such a low level that tetany results. This can be combated by administering intravenous calcium gluconate.

Maintenance of normal sodium plasma levels is important. Normally, the sodium plasma concentration is controlled by the kidney, which is not in operation in anuria. The administration of sodium in any form is rarely indicated, except when there is a deficit such as occurs following vomiting or diarrhea. It may be advisable to measure on occasions the amount of sodium in the vomitus and to replace the exact amount lost. There is an insignificant sodium loss from normal perspiration or bowel movements. There is no substitute for frequent determinations of plasma sodium values. A lowering of plasma sodium from any cause, provided there is normal hydration, results in a shift of water from the plasma into the cells, resulting in intracellular edema. An elevated plasma sodium, on the other hand, such as that following the injection of saline, lactate or bicarbonate, causes a shift in the opposite direction, with consequent hydremia, expansion of the plasma volume, the danger of pulmonary edema, cardiac failure, etc. In addition to the effect on fluid distribution, a low concentration of plasma sodium is not consistent with proper cardiac function. In the past the treatment of acidosis has been overemphasized. Anuric patients in acidosis may have near normal plasma sodium values, and the injection of sodium, either in the form of lactate or bicarbonate, results in expansion of extracellular compartment, a condition which could further embarrass the circulation. The only indication to administer bicarbonate is a markedly lowered sodium plasma level or marked respiratory distress, indicating that the carbon dioxide excretory function of the lungs has reached its capacity.

There is not apt to be a significant disturbance of the sodium plasma concentration within the first or second week of anuria if the patient has been properly managed and if there has been no vomiting, diarrhea, excessive sweating, or unnecessary administration of saline. With the persistence of anuria, the continued catabolism within the cell results in the progressive release of sodium and other electrolytes, making their plasma control increasingly difficult. Plasma chlorides tend to decrease in uremia, but except in case of excessively low values, these compensatory chloride depressions should not be corrected.

In any treatment of anuria, the potassium factor must also be considered. The occurrence of potassium retention and intoxication with urinary suppression has never been appreciated as the serious medical emergency or problem that it represents. During the second World War it was recognized that sudden deaths in anuria were probably due to cardiac arrest as a direct result of potassium poisoning. It is likely that future studies of patients with anuria will reveal potassium disturbances to be a frequent cause of death and that they occur more frequently than believed in the past.

Potassium, usually in combination with protein, is the main cation within the cell. With protein catabolism, potassium leaves the cell, resulting in hyperpotassemia in the absence of kidney function. Plasma potassium concentrations are also affected by plasma sodium disturbances. If, for any reason, the sodium plasma concentration is elevated, sodium then tends to displace intracellular potassium, with a resulting rise in plasma potassium values, especially if urine formation is negligible. When plasma sodium is low, potassium may leave the cell to compensate for this cation depletion. Approximately 90 per cent of the potassium is excreted through the kidneys. If 200 to 300 cc urine is being excreted daily, it is probable that hyperpotassemia will not occur, as the renal clearance of potassium is efficient at that level.

Potassium should not be administered in any form during acute anuria. In the early phases of anuria, the metabolic processes within the body and particularly within the cell tend to bind potassium and prevent hyperpotassemia. As anuria continues over a long period of time, an increasing amount of potassium is released. The administration of glucose and insulin has been advocated to reverse the process and to shift potassium into the cells.

If the total elimination of potassium intake and the reduction of metabolism to a minimum do not prevent toxic plasma levels, measures must be instituted to extract potassium from the plasma and body fluids. In our hospital there have been 15 instances of hyperpotassemia in the last 18 months among several services. Approximately one-half of these died, while 6 of these patients survived as a result of reduction of the hyperpotassemia by intestinal dialysis. Any patient with anuria should have frequent serum potassium determinations, and as the anuria progresses, daily determinations may be necessary. In lieu of a flame photometer, daily electrocardiograms will usually reveal the onset of definite cardiac toxicity. In severe and dangerous serum potassium elevations, the removal of potassium by artificial kidney, intestinal or peritoneal lavage is imperative. Control of electrolytes, however, may finally become unmanageable as a result of disturbances in cell membranes.

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METABOLISM

A number of approaches have been made as to proper diet in anuria. The average individual at bed rest has a daily caloric requirement between 1400 and 2000 calories. A patient without food intake metabolizes about 70 gm. of his own protein a day, but if given 100 gm. of glucose this deficit is reduced to approximately 40 gm. The glucose serves to supply few calories, but its main effect is the reduction of ketosis and protein catabolism. It may also reduce, up to 300 per cent, the formation of unknown toxins and organic acids by aiding in their oxidation. Glucose intake in excess of 100 gm. does not cause a further appreciable reduction in protein catabolism or oxidation of organic acids and merely adds additional calories. With protein catabolism decreased, there is a significant diminution in the amount of potassium liberated from the cell.

As it would be ideal to keep the patient in caloric balance, attempts have been made to attain this end by adding fats to the diet. Mixtures of peanut oil and glucose can sometimes be given by mouth in sufficient amounts to provide 2000 calories a day. This amount of fat and glucose, unfortunately, is likely to produce severe diarrhea, with water and electrolyte loss. We believe it is better for the patient to be in caloric deficit for 2 weeks rather than stress administration of unpalatable fat-glucose mixtures by mouth. If glucose cannot be tolerated perorally, 50 to 100 gm. per day intravenously is a requisite. Most of the published diets contain undesirable proteins, which only increase the formation of toxic metabolic products. The protein and fruit juices in these diets also contain electrolytes, especially toxic potassium.

The patient must be maintained at bed rest in order to minimize metabolism. Vitamins should be administered daily in such periods of dietary restrictions and starvation.

SUPPORTIVE THERAPY

Adjunct procedures such as digitalizing have been recommended, but there is no evidence that, in the absence of heart failure, this is on a sound basis. Since digitalis cannot be excreted, it should be used with caution. Injection of red cells may aid the oxygen capacity of the blood, and there is no contraindication to blood transfusion except in the case of hyperkalemia. Oxygen therapy may occasionally be helpful. Aminophyllin is said to relax bronchial spasm and aid in the elimination of carbon dioxide from the lungs. Infection must be controlled, because it increases the metabolic rate and also greatly accelerates water loss through perspiration from fever.

Diuretics have no place in the treatment of fully-established anuria, and their use in the past has been illogical except as a prophylactic measure. It is important to maintain electrolytic normality within the fluid compartments, and the injection of such diuretic salts as sulfates, nitrates, mercury, magnesium, etc. can result in disastrous disturbances in the electrolytic plasma pattern.

In the great majority of anuric patients treated according to the principles just outlined, there is an onset of diuresis usually before the end of the second or third week. With the employment of such conservative management, the patient is not likely to succumb to water or electrolyte disturbances, thus allowing time for renal repair. A recent report on conservative management in cases of anuria from nephron necrosis has revealed a recovery rate of 85 per cent. In the fatal cases, the patients did not succumb to renal failure but to other complicating factors.

ACCESSORY TREATMENT

In an occasional case, usually one mismanaged or one in which anuria persists for a long period, therapeutic procedures may be necessary to remove metabolites or to correct water and electrolyte imbalances. Accessory modes of treatment of anuria are cross or replacement transfusions, peritoneal and intestinal dialysis, exchange cation resins, and the artificial kidney. The application of these procedures has not been reported in the past in adequate number or in detail for proper scientific appraisal. Emphasis has been placed mainly on the removal of urea and nitrogenous substances. Most reported accessory treatments have been instituted within the early phases of anuria, and in most instances they were not indicated at the time employed. One must disagree with their advocates who conclude that "they have saved the lives of patients." In a correctly managed patient, artificial dialysis is rarely necessary within the first two weeks of anuria. If the anuria continues, the products of metabolic breakdown, both protein in nature and electrolytes, become a difficult problem to control. It is during this period that accessory modes of treatment could be of considerable value in removing the accumulating toxic substances and in readjusting electrolyte concentrations—thus leading to a prolongation of life and extension of the patient's chances of recovery.

If a patient has become overhydrated or is in hypernatremia from injected bicarbonate or saline, it may be necessary to remove excess water and sodium with an emergency dialysis procedure. One will occasionally encounter a dangerous elevation of serum potassium within the first two weeks, especially if the patient has been fed. It may be an urgent matter to reduce this serum potassium immediately by such extraction methods.

We do not believe that cross transfusion or replacement transfusion merits consideration, although some excellent results have been reported. It is more likely that the recovery in such instances was due to good medical management and not related to this specific therapy.

Peritoneal dialysis, intestinal lavage, cation resin exchange enemas, and artificial kidney all have their place, and in individual cases one procedure might be preferable to another. For example, if confronted with abdominal distention or a recent abdominal operation, peritoneal lavage would be contraindicated. With nausea and vomiting the patient might not be able to tolerate a lavage tube in the jejunum, and therefore intestinal dialysis would be impractical. Perhaps it would be well to mention very briefly the problems of each method.

The artificial kidney has excited great interest in recent years, but it is too early to judge its effectiveness. It does have one distinct disadvantage, and that is the considerable technical difficulties encountered in its operation. A highly trained team is required which is available only in large medical centers. Sterility, leaks in the apparatus, hemolysis of the red cells, pyrogens, and the technical control of blood flow all demand constant attention. Heparinization of the patient may be hazardous. The various exchanges between the blood on one side of a cellophane membrane and the bath on the other side occur rapidly, making frequent analyses of the serum electrolytes necessary. Blood volume should be accurately determined before dialysis because of the possibility of rapid fluid exchange across the membrane. The electrolyte composition of the bath in the artificial kidney must be modified in individual cases according to the electrolyte composition of the patient's plasma. The osmotic pressure of the bath must be slightly higher than that of the plasma, so that there will be a flow of fluid from the plasma into the bath. A dialysis of several hours with such an apparatus will undoubtedly correct many metabolic, electrolytic, and fluid disturbances which may otherwise be difficult to control. Because of the above inherent difficulties, the artificial kidney is not applicable in the majority of acute renal failures that occur. Simple procedures are more feasible.

Peritoneal dialysis is a far more simple procedure, but it, too, requires a great many technical considerations. The peritoneal membrane evidently nearly approximates a pure dialyzing membrane. The cells of the peritoneum, however, are living cells, and electrolyte exchanges do not take place quite as freely as through inert cellophane. In the past, peritoneal dialysis has usually been accomplished by the constant inflow of a fluid into one side of the peritoneal cavity with aspiration on the opposite side. This procedure has the advantage of allowing a solution of constant composition to be in contact with the peritoneal membrane. Unfortunately, channeling among the intestinal coils and mesentery occurs, so that only a restricted area of the peritoneum is actually in contact with the perfusion fluid. There may be further difficulty with egress of the fluid. Recent experiences here (to be published) and elsewhere have indicated that the repeated instillation of a fluid of proper electrolyte composition into the peritoneal cavity, where it is allowed to remain for one to two hours, followed by aspiration, is more effective. The fluid evidently is in contact with a greater area of peritoneum. Peritonitis has been a complicating factor, but with antibiotics this is no longer a major complication.

The literature indicates that peritoneal dialysis has not been generally successful, and from the incidence of edema, hyperchloremia, etc. it has not been performed correctly. One can conclude that it has probably not saved many lives; on the *contrary*, many patients have succumbed to the disturbances it has created in the internal chemical and fluid environment. In peritoneal lavage or in any dialysis one may easily dehydrate or overhydrate the patient, deplete or produce excess concentrations of electrolytes, especially sodium and chloride, unless a proper perfusion solution is correctly employed.

Intestinal dialysis can be an extremely valuable adjunct in the treatment of total anuria. The mucosal cells do not act as a simple dialyzing membrane but have dynamic, secretory, and absorptive powers which vary at different levels of the bowel. Glucose, for example, must be hydrolyzed in the intestine before it crosses the mucosal membrane. One simply removes the substances which have been secreted within the intestinal lumen. Intestinal dialysis is a relatively simple way to remove potassium in those cases with hyperkalemia. The jejunum is far more efficient for extracting potassium than other sections of the intestinal tract.

Most patients in the early phases of anuria are able to swallow a Miller-Abbott tube, and in the majority a satisfactory perfusion can be established. Meyers Hicks was able to perfuse the jejunum with 24,000 cc perfusate in one 24 hour period, removing 4 gm. potassium and 49 gm. urea. Urea is an easily diffusible compound, and lavage of the jejunum is efficacious in removing this substance. In lieu of using a Miller-Abbott apparatus, there have been instances in which segments of jejunum have been isolated and lavage carried out through stomas made into the abdominal wall. One remarkable case has been reported by Kolff, who kept a patient alive for 46 days after removal of his only kidney. The patient was also kept in electrolyte and water balance by appropriate adjustment of the content (and ultimately the osmotic pressure) of the perfusing fluid. Death resulted from a thrombus originating in the heart, following feeding of the patient through an intravenous polyvinyl cardiac catheter. During the dialysis, 8.6 gm. of urea were removed per day (a patient in starvation produces about 2 to 4 gm. of urea a day and approximately 6 gm. of nitrogen). Large amounts of creatinine and uric acid were removed from this patient, so that excess plasma concentrations of these substances did not occur during the period of observation. The osmotic pressure of the perfusing fluid was at first less than that of the plasma, and the patient absorbed 8.2 liters of water during the first four days along with 6 to 10 gm. sodium chloride in excess of that which was lost by vomiting. The positive fluid and electrolyte balance was then reversed by increasing the osmotic pressure of the perfusate by the addition of glucose and sucrose. During the next 9 days, 16.4 liters of fluid containing 48 gm. sodium were removed from the plasma, or approximately 1500 cc a day. During this period, 0.8 to 2.4 gm. potassium were extracted per day, reducing the plasma level from 8.0 to 4.3 mEq/L. The patient absorbed sodium bicarbonate from the perfusing fluid in sufficient quantity to keep the plasma bicarbonate at an approximately normal level.

The large bowel is more accessible than the jejunum, but it is not so efficient as the small bowel or peritoneum. The colon has selective resorptive properties so far as water, sodium, and chloride are concerned. Urea and other products of nitrogenous metabolism do not readily diffuse across the large bowel, and a negligible quantity of these substances is removed during lavage. Potassium can be extracted from the large bowel, and in one patient with hyperpotassemia, we performed perfusion through an appendicostomy. We were able to remove 20 mEq of potassium, or approximately the normal potassium content of the blood plasma, with 4 liters of perfusate.

Certain synthetic resins of the ammoniated type which are insoluble in water have a strong affinity for sodium and potassium. When introduced into the large bowel in the form of an enema, they soon bind significant amounts of these electrolytes. One experimenter has recently been able by the use of resin enemas to remove 76 mEq of potassium in a day. Resins are impractical perorally in anuria. When ingested they may disturb electrolyte balance by extracting sodium. If used in retention enemas they may cause obstruction because of their physical nature. In addition, the enema may not be retained.

In summary, then, the particular type of artificial dialysis employed will be governed by the condition of the patient and the available technical facilities. In some instances, they may be used primarily to control potassium, sodium, or fluid disturbances, while in others they are used to remove the accumulating products of catabolism in the later phases of anuria.

Renal decapsulation as an accessory procedure for anuria must be mentioned. Urologists on occasion have decapsulated the kidneys in the belief that the operation diminishes intrarenal pressure. The validity of this procedure is difficult to appraise, and the literature is replete with experiments and arguments both for and against the operation. Reported cases are sporadic, and collateral or accessory treatment is so varied as to complicate any conclusion concerning its efficacy.

Pathological evidence for increase intrarenal pressure is found in the significant observations from the data published by Lucké, who studied more than 700 pairs of kidneys sent to the Army Institute of Pathology following death from anuria. The weight of 89 pairs of kidneys selected at random was considerably more than the normal 300 gm. for a pair of kidneys. It is remarkable that many pairs of kidneys weighed from 500 to more than 800 gm., which is practically double their normal weight. The only factor that could account for this increase in weight is the presence of additional water or edema fluid. In other words, for the kidney to remain normal in size and still to double in weight, water would have to displace some substance which is much lighter. This being impossible, the only explanation is that the kidney is greatly increased in size to the limit of expansion of the capsule, with the result that there could be a significant increase in intracapsular tension. On the other hand, if the anuria in a given instance is due solely to tubular degeneration, then decapsulation would not produce diuresis. If the regenerating tubular cells are capable of function, then additional intrarenal pressure might be just enough to inhibit urine flow, and the release of tension by removal of the capsule could be the deciding factor.

About 6 years ago we performed unilateral renal decapsulation in 7 patients with acute anuria. In 6 out of the 7 cases the kidney was ischemic, greatly enlarged in size, and the capsule was exceedingly tense. The pale white cortex became pink-colored following decapsulation, and in 5 patients there was immediate diuresis, which increased rapidly by the end of 24 hours. Biopsy of the cortex showed varying degrees of tubular injury and obstruction. These patients were *overhydrated* by the time they were first seen, and it may be that the excess intrarenal pressure was purely a reflection of excessive fluid administration. Decapsulation may be of value, therefore, in the overhydrated and edematous patient.

Finally, it would be amiss not to mention a significant feature of the postanuric diuresis during the recovery phase of anuria. Renal function is not normal with the onset of diuresis, and the newly regenerated epithelium is unable to properly reabsorb sodium and especially chloride, resulting in the excessive loss of these electrolytes in the early formed urine. Circulatory failure due either to contraction or expansion of the plasma volume may occur in this critical period. Depletion of serum potassium and calcium may result in tetany. At the onset of diuresis, vigilance must be exercised in this respect.

SUMMARY

Modern and intelligent therapy of the anuric patient with reversible renal injuries should consist of the following program:

1) Body water content should be maintained near normal. Any deviation on admission should be carefully corrected. Total fluid output should be accurately determined and an equal intake balanced against the daily loss.

2) Electrolyte patterns of the internal chemical anatomy must be maintained with as nearly normal concentration as possible.

3) Electrolytes should not be administered in any form, except in case of specific deficits (vomiting, diarrhea, etc.).

4) Sodium should not be injected in any form, except when a definite sodium deficit occurs. Indiscriminate therapy toward counteracting the "acidosis" has been overemphasized.

5) Deviations in the concentrations of the cations, sodium and potassium result in specific deleterious and dangerous effects.

6) Serum potassium elevations may occur with specific toxic effects which are hazardous to cardiac function. In such instances, potassium must be removed by some form of artificial dialysis.

7) Metabolism must be reduced to a minimum to avoid release of potassium, other electrolytes, acid radicals, unknown metabolites, and toxins.

8) Glucose (at least 50 to 100 gm. per day) reduces protein catabolism and expedites the oxidation of organic acids. Glucose *must* be administered daily.

9) The diet should not contain proteins or electrolytes. Fats (peanut oil, butter) combined with additional glucose may be given perorally to provide for the calories in this condition of negative caloric balance, if they do not cause diarrhea. Daily vitamins are required.

10) Infections elevate the metabolic rate and protein catabolism. The fever coincident with infection greatly increases water loss (active perspiration) and complicates the maintenance of fluid balance. Infectious processes should, if possible, be rigidly controlled.

11) Adjunct therapy such as aminophylline, oxygen, and digitalis, except in congestive failure, are of questionable value. Diuretics are contraindicated.

12) Transfusions for anemia are indicated except in hyperkalemia. Plasma may be necessary for depleted serum proteins.

13) Excessive salt loss during the diuresis period must be recognized, with proper replacement as it occurs.

14) Therapy to increase renal blood flow, such as sympathectomy, spinal anesthesia, intravenous procaine, etc., is without evidence of scientific value.

15) Renal decapsulation to relieve intrarenal elevated pressure and increase

renal blood flow could be of value in those cases in which the kidneys are greatly swollen and ischemic. The latter condition occurs only in certain instances, such as after overhydration or an allergic anuria (after sulfa poisoning, etc.).

16) Artificial therapy in the form of exsangino- and cross transfusions has not produced evidence of any real value.

17) The artificial kidney and peritoneal and intestinal dialysis have not proved to save the life of properly managed patients when instituted within the first two weeks after the onset of anuria. Exception to this is their value in removing dangerous serum potassium and sodium as well as excess water in emergency situations in which there is impending cardiac failure. None of these conditions is likely to occur within the first 10 days of anuria if management has been fundamentally correct from the onset. The removal of urea and other nitrogenous products by artificial means in this period has been successful but unnecessary. If anuria proceeds into the third and fourth week, products of protein catabolism may accumulate to such proportions as finally to jeopardize life. These consist of organic acids, other metabolites, and unexcretable electrolytes. The institution of any one of the dialyses will remove large amounts of such nitrogenous products, electrolytes, and water as desired. No one form of dialysis has a distinct advantage in all respects over the other. Each has its indications and limitations. Each may be indicated in a given or specific case. If applied when actually needed, each may be useful and may prolong life.

CONCLUSION

Patients with anuria who are kept in proper electrolyte and water balance with a nearly normal internal chemical environment will live up to three weeks or longer with few, if any, symptoms of uremia. In this period of time, the renal injuries if reversible usually will heal. An analysis of the literature strongly suggests that most deaths from anuria may have been due to misdirected therapy. In certain selected instances and especially in cases in which anuria persists into the third week, some form of artificial dialysis may correct deviations in electrolytes, water, and metabolites with prolongation of life and increase in chances of recovery of the patient.

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RENAL INSUFFICIENCY: ITS MECHANISM AND MANAGEMENT

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To the urologist today renal insufficiency furnishes opportunity for participation in a broad field of endeavor. The previously bizarre picture of clinical uremia has taken a form, the outline of which is composed of certain pathologic and physiologic facts. The various types of anatomic lesions of the kidney are known to produce definite changes in the circulating blood, extracellular fluids, intracellular fluids, and the urine. A great deal is known about cause and effect, but much remains to be learned with regard to intermediary mechanisms within the kidney itself and within the intracellular and extracellular fluid compartments of the body.

There are yet many details which remain to be discovered to complete the picture. These can only be determined by the co-operative efforts of the investigators in the laboratory, the ward, and the clinic working actively together for the welfare of the patient. The urologist is in the secure position of having the accurate definitive measures at his disposal for beginning the drawing of the picture of renal physiology and the nature of the renal pathology or as the case may be, the absence of renal disease.

Uremia literally means an accumulation of the constituents of urine in the circulating blood, but the clinical connotation which has evolved indicates a state of toxicity caused by retention of nitrogenous and other waste products with an accompanying upset of fluid and electrolyte balance. The failure of normal elimination by the kidney may result either from so-called prerenal factors such as circulatory, metabolic, and hepatic disease or from primary renal disease. The latter may be intrinsic or may be induced by processes originating beyond the kidney and exerting a deleterious effect upon it. This presentation, however, is concerned with the mechanisms of development and the management of renal insufficiency due to those conditions having urologic implications. The urologic problems of the uremic patient are caused notably by obstruction and infection (pyogenic and tuberculous) which are predisposed to by congenital abnormalities, urolithiasis, neoplasm, trauma, and vascular disease. The management of these problems is primarily directed toward relief of obstruction, restoration of renal circulation, and prevention of spreading infection in order to regain homeostasis.

It must be emphasized also that modern methods of diagnosis and therapy occasionally may induce anuria in the patient with antecedent unrecognized renal disease. Pyelographic investigation, sulfonamide treatment, transfusion of blood, and major surgical procedures have each been prominent factors in the history of patients hospitalized because of anuria. Severe renal insufficiency may complicate surgery of the solitary or previously diseased kidney as well as other forms of major surgery especially of the biliary tract when hemor-

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rhage, shock, or sepsis has supervened. The early recognition of prerenal azotemia complicating postoperative convalescence is urgent and at times difficult. Undesirable reactions to all of the antibiotics may occur and result in profound disturbances of water and electrolyte balance. Severe diarrhea has been a prominent feature in patients having a toxic reaction to antibiotics and the physiologic electrolyte disturbance caused thereby has resulted in circulatory and renal failure. Uremia, following ureterosigmoidostomy, may be due to ureteral obstruction and to reabsorption of certain constituents of the urine by the bowel. The latter condition usually results in hyperchloremic acidosis with hypokalemia.

THE PATHOLOGIC PHYSIOLOGY OF RENAL INSUFFICIENCY

Any condition which interferes with the normal circulation of blood through the glomerular capillaries diminishes total renal function. Disturbance of the excretory units or tubules also results in alteration of the normal functional capacity of the kidney. Both vascular and excretory units may be damaged by processes obstructing the conducting pathways of urine away from the kidney. Infection of the renal parenchyma causes edema, congestion, suppuration, and eventually necrosis with complete destruction of all portions of the nephron if allowed to progress. Anoxia and ischemia occur from the development of arterial and venous thrombi complicating overwhelming infection, phlebothrombosis, and extraneous toxins. Intratubular deposition of acid-heme products and methemoglobin from extensive hemolysis renders a cessation of excretory function and interference also with glomerular filtration. Sulfonamide crystalluria likewise causes tubular occlusion as well as ureteral obstruction.

Pursuant to major surgical procedures there are certain postoperative changes in renal function which are influenced by the following facts: There is a diminution in the ability of the kidneys to excrete sodium which is attributed to the stress reaction with its release of desoxycorticosterone-like substances by the adrenal. The liberation of excessive amounts of norepinephrine by the adrenal contributes to renal arterial vasoconstriction and oliguria or anuria. Sodium retention results in water retention as well as a disturbance of electrolyte balance and protein metabolism. At the same time varying degrees of renal arterial vasoconstriction occur which are more severe if significant hypotension and hemorrhage have complicated the operation. These factors produce renal ischemia and anoxia with profound disturbance of total renal function the details of which will be discussed later. A blood transfusion reaction in the presence of pre-existing shock is more likely to result in severe tubular damage and anuria than if hypotension has not been present. A valuable contribution has been made by Rosoff et al. in this regard in studying the effect on the kidney of the injection intravenously of the degradation products of hemoglobin in the presence and absence of shock. Furthermore the stress reaction, fever, and infection each causes an increase of protein catabolism especially during the postopera-ve period when there is an inadequate caloric intake. Protein catabolism lts in the liberation of excessive amounts of potassium from cells into the interstitial fluids and the serum of the blood. Coincident oliguria or anuria results in hyperkalemia and this excess of extracellular potassium quickly interferes with myocardial function and will be fatal if not promptly corrected.

Vomiting, diarrhea, adynamic ileus and fever bring about profound alterations of acid base balance which further increase the grave significance of renal failure in the postoperative patient. Prolonged vomiting depletes the extracellular stores of chloride and the measurement of the plasma chloride shows it to be well below the normal level. If no sodium is lost, but chloride alone, then some other anion must be increased in order to maintain the proper electrolyte (cation-anion) balance. This is spontaneously accomplished by expansion of the bicarbonate content of the plasma and the rest of the extracellular fluid in order to cover the chloride loss. The mechanism by which the bicarbonate fraction has increased to compensate for chloride loss is through the retention of carbon dioxide by its conversion to the bicarbonate ion. The respiratory mechanism thus rapidly and effectively compensates for chloride loss from the stomach. However, if renal failure and acidosis exist, the respiratory mechanism has to decrease the bicarbonate content of the blood to compensate for the renal retention of other anions such as sulfate and phosphate. The lungs lower the carbon dioxide content of the extracellular fluids by deep gasping respirations of the Kussmaul type to meet such demands.

Perhaps the most important way by which the body regulates its content of fluid, acid, and base is by the normal functions of the kidney. In this regard renal function serves the purposes of excretion of waste products of metabolism, the regulation of acid and base composition of body fluids and the control of water balance simultaneously. The normal kidney performs these functions admirably and several simple tests of renal function indicate its attempt to perform this function when needed. This function is illustrated in the conservation of fixed base by the kidney under the stress of acidosis as it concurrently excretes the acid products in the urine in larger amounts than usual with a weaker base, namely ammonia, which is formed in the kidney. The strongly acid urine represents an attempt by the kidney to spare base for the body and may be noted at the bedside by using nitrazine paper to determine the hydrogen ion concentration. The converse may be noted in the patient with alkalosis following loss of hydrochloric acid in severe vomiting wherein the kidney selectively attempts to retain chloride and does not substitute ammonium and hydrogen ions for sodium so that a strongly alkaline urine is excreted.

The concentrating power of the renal tubules and their ability selectively to reabsorb both water, organic and inorganic solutes are major functions. The regular determination of the specific gravity of the urine on the ward or at the bedside constitutes the simplest of tests which is equally as neglected as the measurement of the hydrogen ion concentration. The normal kidney responds to the stress of water deprivation or dehydration by attempting to spare water for the body and yet at the same time excrete the usual daily load of 30–35 gm. of solid metabolites in a smaller volume of highly concentrated urine. Where tubular damage has occurred by any of the processes previously mentioned, rhage, shock, or sepsis has supervened. The early recognition of prerenal azotemia complicating postoperative convalescence is urgent and at times difficult. Undesirable reactions to all of the antibiotics may occur and result in profound disturbances of water and electrolyte balance. Severe diarrhea has been a prominent feature in patients having a toxic reaction to antibiotics and the physiologic electrolyte disturbance caused thereby has resulted in circulatory and renal failure. Uremia, following ureterosigmoidostomy, may be due to ureteral obstruction and to reabsorption of certain constituents of the urine by the bowel. The latter condition usually results in hyperchloremic acidosis with hypokalemia.

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PHYSICAL EXAMINATION

The physical examination of the uremic patient yields much valuable information. The degree of toxicity manifested in the patient's facies is important. Dryness of the skin and mucous membranes is the rule in the chronic uremic and paleness due to secondary anemia is a frequent concomitant. The patient in early acute uremia, however, whose fluids have been managed properly, may be adequately hydrated and also may show no anemia. The cyclical Cheyne-Stokes respiration is a manifestation of the terminal stages of the condition. General anasarca as well as pulmonary edema signifies circulatory failure and that excessive amounts of fluid and sodium chloride have been administered. Hepatic enlargement and jaundice may indicate the presence of a prerenal factor as a cause of uremia. Enlargement of the kidneys on one or both sides may be present as a result of pyelonephritis, pyonephrosis, hydronephrosis, diffuse renal engorgement, neoplasm, and polycystic disease.

In the case of obstruction in the urethra or at the bladder neck by enlargement of the prostate, the bladder may be palpated to the umbilicus or higher. Rectal examination may reveal an enlarged benign or malignant prostate causing vesical obstruction or other neoplasms in the pelvis causing ureteral obstruction such as retroperitoneal lymphoma or carcinoma of the rectum. In the female patient, carcinoma of the cervix is a common cause of bilateral ureteral obstruction and uremia. This as well as other neoplasms in the pelvis may be discovered by combined pelvic-abdominal and recto-abdominal examination. The examination of the extremities is of importance in uremia with reference to edema, phlebothrombosis, and signs of advanced cardiovascular disease. Measurement of the blood pressure often reveals a striking degree of hypertension in both chronic and acute uremia, which may be regarded as either a causative or a compensatory physiologic phenomenon depending upon the etiology of the condition. The finding of hypotension in the presence of uremia is an ominous sign which indicates poor renal circulation and a failure of the cardiovascular system to compensate for and to meet the physiologic demands created by the underlying disease process.

MEASUREMENTS OF RENAL FUNCTION

Detailed urinalysis gives information regarding the hydrogen ion concentration, the degree of proteinuria, pyuria, bacteriuria, and of particular importance, the specific gravity of the urine which reflects the concentrating power of the renal tubules. An accurate measurement of the fluid intake and output correlated with the specific gravity of the urine and the daily weight of the patient furnish a simple control in the proper day to day administration of fluids. Estimation of insensible fluid loss and added increments from fever as well as vomiting and diarrhea must be made. Phenolsulfonthalein excretion serves as a measure of tubular function and may be supplemented by urea and creatinine clearance studies. Glomerular filtration rates may be measured by inulin and para-aminohippurate clearance. The daily or alternate daily determination of the blood urea nitrogen, carbon dioxide combining power, serum chloride and the hematocrit yields basic information necessary for the proper regulation of fluid and electrolyte balance in severe renal failure. In special instances of anuria or severe oliguria wherein hyperkalemia is suspected, an electrocardiogram and determinations of the serum potassium and sodium are also necessary. Hyperkalemia is a hazard chiefly when anuria is present. Serum proteins, hematocrit and hemoglobin content must be determined from time to time in patients having chronic uremia, and measurement of the albumin-globulin ratio is helpful in those patients having edema. By making a simple chart on a single sheet of paper showing the minimal studies, the day to day determination of the fluid and nourishment to be administered is regularly determined.

UROLOGIC AND ROENTGENOGRAPHIC EXAMINATION

One of the most valuable and fundamental roentgenographic examinations is the plain film of the abdomen. This basic examination serves as a control to be compared and contrasted with subsequent examinations in which instruments or opaque media are used. The so-called plain urogram should be made as soon as possible. This delineates the renal shadows and shows at once discrepancies in size, shape, and position of the kidneys. Simple urethral catheterization confirms the presence or absence of vesical retention of urine. If the patient is in chronic urinary retention due to vesical obstruction, urethral catheter drainage with a No. 14 or 16 gum rubber balloon catheter should be instituted. The plain film will also show alteration of the ileopsoas muscle, opacities due to calculi and evidences of adynamic ileus, peritonitis or intestinal obstruction. If there is evidence in the history or upon physical examination of ureteral obstruction from intrinsic or extrinsic causes, cystoscopic examination and ureteral catheterization are indicated. In general, pyelography is unwise in the uremic patient. However, according to special indications from time to time, retrograde pyelograms may be done without injury and yield valuable information. Under no circumstances should excretory urography be used in the uremic patient. It is hazardous by virtue of throwing a foreign substance into the blood stream which the already damaged kidney must attempt to excrete. In addition, the damaged kidney is unable to concentrate sufficiently to give any information other than that no visualization of the collecting system is obtained. In the case of strictures of the urethra gentle instillation of opaque 20 per cent skiodan, rayopaque or lipiodol into the urethra will accurately locate the position and relative size of the stricture. Calibration of the urethra with filiforms and followers, the emptying of the bladder and placing the patient on constant drainage are, of course, at once indicated. Any necessary dilatation or surgical intervention should be postponed ideally until after a period of drainage which allows for re-establishment of renal and circulatory equilibrium to a maximal degree and affords the opportunity for protection against spreading infection by appropriate antibiotic or chemotherapy. The importance of minimal instrumentation and gentleness in the management of the severely ill patient cannot be overemphasized.

GENERAL PRINCIPLES OF MANAGEMENT OF RENAL INSUFFICIENCY

A. Urologic treatment. The urologic treatment of the uremic patient is directed toward preservation of renal parenchyma, restoration of renal function, and control of infection. When an obstructive lesion is responsible for uremia, adequate drainage must be instituted by the simplest means possible. Urethral drainage of the bladder with a small (14F or 16F) gum rubber catheter is well tolerated in practically all cases. When the urethral catheter will not pass or when it is not tolerated well, a suprapubic catheter is inserted under local anesthesia unless a stricture is present which demands external perineal urethrotomy. The total collection, measurements, and examination of the urine each day are of primary importance. Ureteral drainage in cases of obstruction by stone and infection may be life-saving initially and permit restoring the patient to satisfactory condition for definitive surgery. We have found that prolonged ureteral drainage is best accomplished by means of polyethylene catheters. Their inertness confers excellent tissue tolerance, the enlarged lumen of the catheter permits maximal drainage and the failure of blood to clot and of lime salts to be precipitated in them has resulted in very effective drainage. We have utilized the inlying polyethylene ureteral catheter continuously for as long as four weeks. When urethral obstruction prevents the passage of a catheter, ureterostomy, pyelostomy, or nephrostomy, unilateral or bilateral as indicated, must be carried out. In such cases of bilateral ureteral obstruction caused by cancer of the urinary bladder, prostate, or uterine cervix, careful studies should be made in order to determine which kidney has been obstructed the shortest length of time and is therefore presumably the better of the two organs and hence the one to be drained first. At times ureterosigmoidostomy or ureterocutaneous transplantation may be chosen instead of nephrostomy or pyelostomy when ureteral catheterization fails.

The choice of anesthesia in uremic patients is of major importance. Local anesthesia supplemented with preliminary analgesia has been ideal for nephrostomy and pyelostomy; continuous spinal anesthesia is effective and safe if carefully regulated. Anoxemia is avoided in maintaining an adequate airway and by administering oxygen in high concentration with nitrous oxide or ethylene in small amounts to minimize the hazard and increase the facility of the operation. Minimal tissue trauma, hemostasis, and maintenance of the circulating blood volume and blood pressure enable one to bring these seriously ill patients through surgical intervention successfully. Where operative intervention is elective it is at times indicated to prepare the patient for surgery by means of external dialysis with the artificial kidney. This form of treatment may be of great value when instituted during the postoperative period in order to give transitory relief of the burden imposed by operation upon the already damaged kidney.

B. Fluid and electrolyte regulation. A primary problem in the treatment of renal insufficiency is the determination of the proper volume of fluid to be administered. An approximation for insensible water loss may be ascertained by using the figures determined for this by Gamble. Under basal conditions about 0.6 cc of water per kilogram per hour is lost by evaporation and respiration. For a 70 kilogram patient this equals about 1000 cc in 24 hours. To this must be added the volume of urine, vomitus, intestinal drainage, and fluid lost by diarrhea. With fever or obvious sweating the basal loss may be increased by 100 per cent. For each degree of fever an added increment of 0.1 cc per degree of fever per kilogram may be added as fluid lost. Daily weighing of the patient is necessary in order to complete the picture of how the fluid and caloric balance is being maintained. If the caloric intake is inadequate, then a gain in weight or even maintenance of a constant weight must represent overhydration with attendant hazard of edema and congestive heart failure.

Maintenance of an adequate caloric intake is necessary to prevent endogenous protein catabolism with the resultant liberation of nitrogenous metabolites which the damaged kidneys cannot excrete. It is difficult to administer such an intake by parenteral means in a limited volume of fluid. It is a distinct advantage if the patient is capable of getting his nutrition by oral ingestion. In the face of anuria a restricted protein potassium free diet is indicated. One hundred or more grams of carbohydrate must be given within the fluid requirement. Gastric losses are replaced by isotonic saline and small intestinal losses by sodium bicarbonate or lactate and saline in isotonic proportions by volume for the maintenance of a normal anion-cation ratio. Water soluble and fat soluble vitamins are of especial importance during the period of parenteral feeding and until normal dietary habits have been resumed. They are easily given by parenteral means. Fat is the most concentrated source of calories available by either the oral or intravenous route and therefore is a greater sparer of protein than is carbohydrate. Extensive studies of the use of intravenous fat in the nutrition of the surgical patient have been made by Stare, Moore, and associates. Purification has resulted in its having diminished toxicity and in rendering no damage to the kidney. It promises to be of great value in the acutely uremic patient during the period before eating can be resumed. All measures such as intestinal dialysis by lavage and drainage, peritoneal dialysis and external dialysis by means of the artificial kidney which brings about a quick improvement in uremia and its accompanying electrolyte disturbance hasten the resumption of eating and drinking.

The anabolic effect of testosterone propionate diminishes protein catabolism thereby effectively combating the accumulation of retained nitrogenous waste products. Twenty-five to fifty milligrams daily are given intramuscularly to the adult patient for 4 days and a maintenance dose of 25–50 mg. every other day thereafter during the period of acute renal failure. Active infection complicating renal failure is a serious cause of further protein breakdown and requires accurate careful antibiotic therapy. Sulfonamides should not be used when renal insufficiency is present owing to the absence of any other method of elimination of these compounds from the blood.

When nephritic edema has become a problem without evidence of cardiac failure the cautious administration of 5–10 gm. albumin intravenously is efficacious in obtaining diuresis in the patient who is not anuric. Hypertonic dextrose serves well in a similar manner as a diuretic and as a source of calories.

Once diuresis has been accomplished for the oliguric or anuric patient, extreme sodium chloride loss may occur by way of the kidney necessitating measured replacement. The rate of salt deprivation can be accurately determined by serum and urinary sodium, potassium, and chloride studies. The condition can usually be controlled by adding 5–10 gm. of salt to the diet but severe hyponatremia and hypochloremia require hypertonic sodium chloride for quick replacement. Daily weighing of the patient continues to be an important control on the volume of fluid intake during this period.

Acute potassium intoxication occurs suddenly in the anuric patient and may quickly be fatal. It should be expected in the patient who has been anuric for several days and will be heralded usually by profound weakness and a shocklike state with or without cardiac arrhythmia. The electrocardiogram shows characteristic changes that are diagnostic and immediate therapy is instituted. The serum potassium level will be found in the range of 7–8 milliequivalents per liter. The following measures are of immediate value:

a. Dextrose solution 20 per cent in 200 cc of saline or water with 20 units of insulin added are given by vein.

b. Combat acidosis with 6 gm. sodium bicarbonate in 200 cc distilled water by vein.

c. Calcium gluconate 1 gm. intravenously.

d. Careful administration of 5 per cent dextrose and saline is continued slowly and cautiously to combat dehydration. If serum sodium determinations show hyponatremia, hypertonic saline may be given with benefit.

The effect of the aforementioned therapy will be transitory if the anuric state persists. It will permit necessary surgical intervention in some cases when anuria is on an obstructive basis. However, persistence of anuria for nonobstructive conditions not requiring surgery is then a definite indication for external dialysis with the artificial kidney if available and if not then intestinal or peritoneal dialysis may be used.

During the past 3 years at the Peter Bent Brigham Hospital an extensive experience has been obtained with the Kolff type of artificial kidney by Thorn and Merrill. The effect of external dialysis upon a wide variety of conditions complicating urologic surgery have been studied. Five patients were admitted to the hospital in acute renal failure following transurethral resection of the prostate in which distilled water was used as the irrigating fluid. Two of these patients recovered completely and despite dialysis three died still in anuria although there was transitory clinical improvement following each treatment. A number of these patients have been treated successfully by means of regulation of fluid and electrolyte balance without the necessity of external dialysis. It is our conviction that distilled water should not be used as the irrigating medium in transurethral prostatectomy. Three patients were admitted to us in anuria following nephrectomy. Two of these recovered completely following dialysis and one died some weeks later in uremia. Three patients having anuria as a result of sulfadiazine therapy were successfully managed by ureteral catheter drainage and external dialysis. Many such patients have been successfully treated by conservative means alone but when potassium intoxication threatens a cardiac death the artificial kidney becomes a life saving instrument. Three patients being anuric as a result of an acute exacerbation of chronic pyelonephritis showed marked improvement after dialysis and prolongation of life was accomplished. One patient expired 18 months after treatment; one, 7 months; and one is living and well 6 months later. External dialysis for renal failure as a result of polycystic disease has been utilized in 1 case with transitory improvement. Two patients anuric after total cystectomy and ureteral transplantation to the bowel have been treated. One of these excreted 2000 cc urine into the rectum within 24 hours after dialysis. Several patients have been prepared for operation in the face of severe renal failure and the period of hospitalization greatly shortened by so doing. One patient, who two years previously had been prepared for an operation upon an impermeable stricture of the urethra by two months of conservative therapy, was prepared successfully for surgical intervention on the second admission within a few days by means of external dialysis. In the case of patients having bilateral renal calculi, pyelonephritis, and renal failure, it is possible to improve greatly their condition in preparation for operation and also there is a great security to the surgeon to know that should anuria supervene postoperatively, help can be obtained by this means.

When an hemolytic reaction to blood transfusion occurs, the patient should be given immediately 6 gm. sodium bicarbonate intravenously in 200 cc of fluid. This will minimize hemolysis and hemoglobinuric nephrosis. If this measure fails to prevent anuria, limitation of fluids and balanced electrolyte administration with day to day observations as outlined previously may accompany successful therapy. These measures failing, within three to four days in 20 cases external dialysis has resulted in complete recovery. Four patients were admitted to us in a state of anuria which occurred following excretory and/or retrograde pyelography when an antecedent acute and chronic pyelonephritis was present. In each of these cases a quick successful result was obtained by means of dialysis. Investigation of the efficacy and efforts toward simplification of this method of treatment deserve further attention.

The specific uses of the artificial kidney may be listed according to the experience at the Peter Bent Brigham Hospital as follows:

a. Acute anuria not responding to conservative measures in which the patients' well-being may be maintained by repeated dialysis until a diuresis occurs.

b. For treatment of potassium intoxication.

c. For refractory hypotension, e.g., in biliary and hepatic disease.
d. For severe renal failure before or after surgery.
e. For selected cases of pulmonary edema caused by electrolyte imbalance.

The contraindications to external dialysis are bleeding, acute coronary artery disease, acute myocardial failure, and acute glomerulonephritis.

The surgeon must recall the sodium retaining effect of general anesthesia and operation. Sodium chloride infusions should not be given routinely on the day of operation because the postoperative kidney does not excrete these ions readily. Early mobilization of the patient is important in preventing venous thrombosis and in sparing protein breakdown also. Every precaution should be taken to avoid hemolysis from drugs, distilled water, and incompatible blood transfusions. Avoidance of shock and prompt treatment when it does occur will diminish the postoperative incidence of renal insufficiency.

SUMMARY

The pathology, pathologic physiology, and urologic management of renal insufficiency have been discussed. The general principles of fluid, electrolyte and diet administration appropriate for the treatment of renal failure have been outlined and illustrated by specific cases. The indications for and contra-indications to external dialysis with the artificial kidney have been given.

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LUMBAR URETEROLITHOTOMY

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It is not the purpose of this paper to discuss the technique of lumbar ureterolithotomy. Instead, we wish to emphasize the advantages of using this procedure in the early management of ureteral calculi and stress once more the simplicity of this definitive procedure in the interception of ureteral calculi prior to their lodging in the pelvic ureter. Hippocrates swore that he "would not cut for stone even for patients in whom the disease is manifest." We wonder if we, as urologists, are not taking this oath too seriously. Surgery for stone in his time was undoubtedly a brutal procedure. We believe that the technical advances in surgery today would make him reverse his decision. Do we cut for stone as often as we should? Do we always safeguard the welfare of the patient by instrumental removal of calculi as completely as by surgical removal?

Great credit is due those urologists who have developed a variety of instruments to aid in the passage and extraction of ureteral calculi. These instruments are most successfully used when the calculus is present in the lower ureter. When employed with gentleness and judiciousness, they are reasonably safe. The manipulative treatment of ureteral calculi has become generally accepted and considered today the conservative management of ureteral calculi. The avoidance of open surgery is a wholesome attitude, but we doubt that it is always a wise one. Conservatism in the management of ureteral calculi should connotate no immediate or remote adverse sequelae. We believe that the total welfare of the patient is not always given due consideration as regards complications that occasionally follow this method of removing ureteral calculi.

We would like to review hastily 4 case histories to emphasize this point.

CASE REPORTS

Case 1. W. R. (U.H. 303042) a white man 28 years of age, complained of repeated attacks of pain in the left flank over a period of 2 weeks. A small stone was present in the mid-ureter. It moved into the pelvic ureter following catheter drainage. Several unsuccessful attempts were made to remove the stone by manipulation. The patient had chills, fever and pain in left kidney region. We were never able again to pass a catheter beyond the calculus in the lower ureter. The left pelvic ureter was exposed surgically and found to be injected, firm and edematous. This made palpation of the small stone impossible. The ureter was opened and the stone located near the intramural portion with an instrument. The bladder was then opened and a small sound introduced into the ureteral orifice. Contact with the stone was accomplished, but we were unable to grasp it. Another sound was introduced into the meatus and when it was withdrawn, the mucous membrane of the ureter everted and with it the stone. The stone was the shape of a carpet tack and the point was buried in the wall of the ureter.

Read at annual meeting, North Central Section, American Urological Association, Toledo, Ohio, October 5, 1951.
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The patient's immediate recovery was complete. Eighteen months later nephrectomy on the same side was done because of obstruction.

When we first saw this patient we could have removed this stone easily through a lumbar incision. We waited and manipulated it. This resulted in a major surgical procedure and late pathologic changes in the lower ureter that ultimately destroyed his kidney.

Case 2. J. P. (U.H. 332796) a white man 38 years of age complained of pain in the left lower quadrant and left flank pain. A small stone was located above the pelvic brim. The stone was removed by manipulation. He had chills and fever which proved to be the beginning of peri-ureteral abscess. The abscess was surgically drained. He recovered slowly but completely. Fifteen years later he was examined and found to have an obstruction in the lower ureter and infected hydronephrosis. It will be necessary ultimately to remove this kidney. This is another example of the successful conservative treatment of a ureteral stone with a late result which could have been avoided by lumbar ureterolithotomy.

Case 3. M. B. (U.H. 468660) a white woman 22 years of age had a stone in the right ureter above the pelvic brim. In attempting to aid the passage of the stone with a Dourmashkin bag, rupture of the ureter and urinary extravasation occurred. The ureter was immediately exposed and drainage instituted. Recovery was uneventful.

The stones in the foregoing cases were all aided in their passage into the lower ureter. Our mistake arose from the assumption that we were being conservative. Fortunately, the first 2 cases were seen early in our practice and have made us fearful of manipulating any stone which we think will pass spontaneously. Unless they are very small, we believe they should be intercepted surgically before reaching the lower third of the ureter.

Case 4. P. W. (U.H. 475035) a white man 36 years of age was seen on June 23, 1947. He complained of pain in the right kidney region which he stated was due to a stone in his ureter. He first experienced a severe attack of pain in January 1947, at which time a diagnosis of stone in the upper ureter was made. He was intermittently treated elsewhere from January to April by dilatation of the ureter with Dourmashkin bag to aid the passage of the stone. He suffered severely following each dilatation. His last dilatation was in April 1947. Following it he had chills and fever and was very sick for 2 weeks. On June 1, 1947, he had another attack of pain with fever which had persisted for 3 weeks. A plain urogram showed a normal outline of the right kidney and a faintly outlined globular mass below it. Excretory urography showed poor function of the right kidney, but the mass was more definitely outlined. Retrograde studies showed infection of the kidney and moderate hydronephrosis. The lower pole of the kidney and ureter were pushed laterally. The upper ureter was constricted for about three inches. At operation a thick walled globular, cystic mass about 3 inches in diameter was encountered. On the posterior and medial side of the ureter another mass 5½ inches in length and 1½ inches in diameter was found. The ureter was tightly compressed between these masses (fig. 1). We thought that we were able to squeeze some of the contents of the globular mass ito the ureter. Both masses were difficult to dissect from the surrounding tissue. The oblong mass was tightly adherent to the vena cava so that only the free portion of it was cut away. The globular mass had a very small opening into the lumen of the ureter. The kidney was removed. Pathological report: "The cyst wall consists of partially hyalinized fibrous tissue with a moderate inflammatory process present. No evidence of an epithelial lining can be seen. Diagnosis: Hygroma."

We believe that these cystic masses were due to rupture of the ureter. They were not congenital diverticula or cysts, nor were they peripelvic or lymphatic cysts.

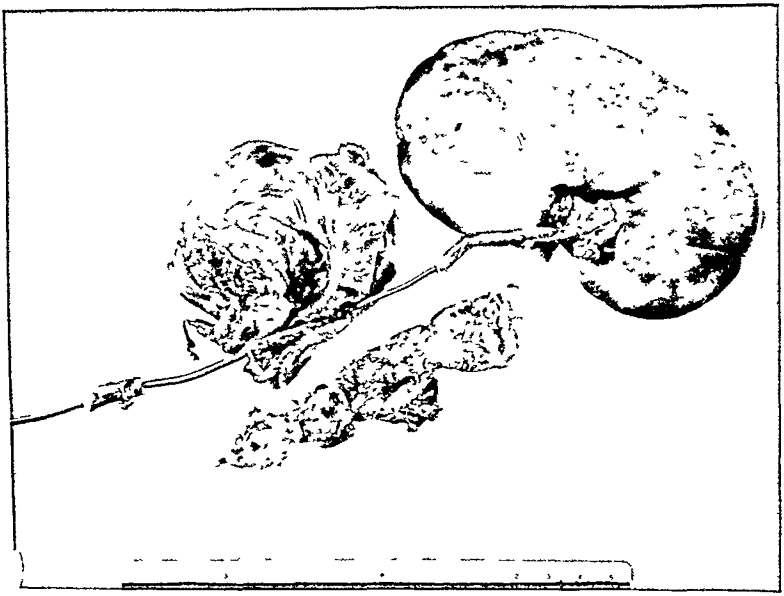

FIG 1

Certainly this is not a conservative treatment of ureteral stone. The kidney could have been saved by early surgical removal of the stone. Accidents such as these have made us fearful of instrumental manipulation of ureteral calculi. Our enthusiasm has been further dampened by the pain, infection, and slow recovery of many patients in whom the stone was removed by manipulation without apparent damage to the ureter. Delayed recovery is probably due to divulsion of the ureter with hemorrhage and infiltration into the ureteral wall and peri-ureteral tissues. Such trauma produces scar and possibly obstruction later.

The muscle-cutting lumbar incision for stone in the upper ureter has always seemed to us to be out of proportion to the offending entity. This idea probably sponsored the development of instruments for removing ureteral stones nonsurgically. A less extensive incision with less trauma was needed to approach the upper portion of the ureter. Foley[1] in 1935 developed a splendid technique for the surgical approach to the upper ureter. We will not describe his technique in detail here but bring out the salient points of it. No muscle is cut or split, each one is dissected free from the underlying muscle down to the lumbar fascia,

[1] Foley, F E B J A M A 104: 1314, 1935

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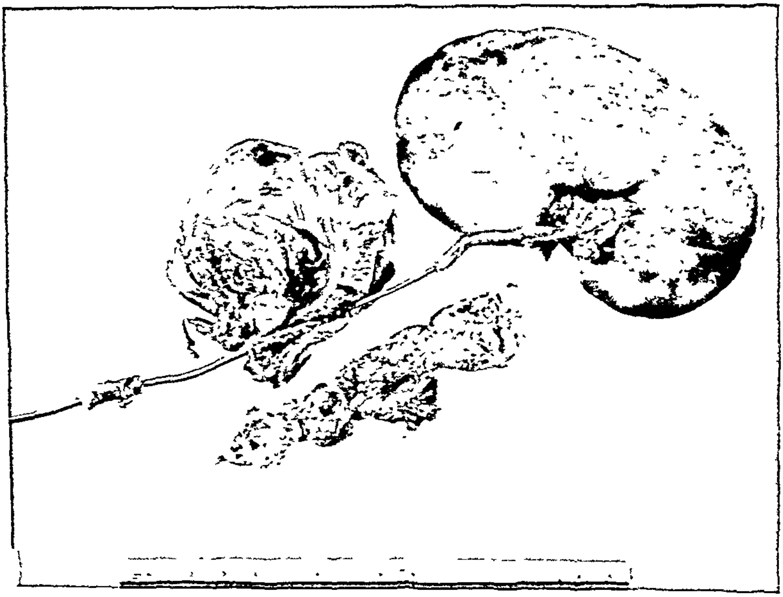

Fig. 1

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[1] Foley, F. E. B., J. A. M. A. 104: 1314, 1935.

which is split in the direction of its fibers. The pararenal (Gerota's) fascia, which lies immediately beneath it, is bluntly dissected from the posterior wall of the abdomen to the vertebral bodies or to the site of the stone. The ureter at the site of the stone is immobilized, incised, and the stone removed. The ureter is closed tightly, as is the lumbar fascia. No drain is used. Skin closed. Our technique varies from Foley's in that we split the external and internal oblique muscles in the direction of their fibers anterior to the border of the latissimus dorsi. We do not close the ureter tightly and always drain. We hold no brief for it over other techniques. It is easy to perform and gives adequate exposure. We have had no complications following its use.

Dees[2] has reported 39 cases of ureteral stone removed by the Foley technique and advises its use for the drainage of perirenal abscesses and biopsies of the kidney. Prince[3] has recently reported the removal of 14 ureteral calculi and a modification of Foley's technique. Barelare[4] has used the operation for various procedures on the kidney and upper ureter 13 times.

Our first attempt to lessen the trauma of cutting the lumbar muscles to remove a stone from the ureter was done June 7, 1937. J. C. (No. 342732) a white man 35 years of age, had had several attacks of colic, due to a small stone in the upper ureter, for 8 days. He was completely relieved by catheter drain of his kidney for one day and demanded his release from the hospital. Two days later, he returned and demanded that the stone be removed. At operation we cut the anterior border of the latissimus dorsi and split the remaining structure. A small stone 4 by 6 mm. was easily removed. The patient left the hospital on the ninth postoperative day. Five other patients were operated in the same manner with an average hospital stay of 8 days.

We have performed a muscle splitting operation 44 times upon 43 patients. Twenty-nine were males and 14 females. Forty-two were white and one, a Negro. The stone was in the right ureter 17 times and in the left 27. One patient had a stone removed from the right ureter and one year later he returned with a stone in the left ureter and was operated on within 7 hours after the attack began. In both incidents he left the hospital in 4 days. The shortest postoperative hospital stay was three days. Our only complication occurred in a very obese, diabetic patient who developed a wound infection which necessitated her remaining in the hospital 20 days postoperatively. Another patient with a stricture in the ureter wore a T tube 21 days. The average postoperative stay in the hospital was 7 days, including the last two cases. The stones were located in the mid-ureter 25 times, upper ureter 18 times and in the kidney pelvis once. Twice during an operation the stone escaped into the kidney pelvis. In the first case, the stone was withdrawn through the ureteral wound, but a pyelotomy was necessary to remove it in the second case. In neither case was the incision enlarged. We found it a very valuable procedure in 3 patients with a single kidney and one that was 6 months pregnant.

We have failed to remove the calculus by lumbar muscle splitting ureterolithotomy in four patients. In one patient with a single kidney the stone moved down beyond our reach. In another patient the stone moved up into the kidney pelvis. In two other patients the stone could not be located visually or on palpation. In each instance, the incision was widened by cutting the muscle. These cases are not included in the 44 cases in which the incision was not enlarged. We do not wish to convey the idea that all calculi should be removed surgically, from any part of the ureter. A review of 348 cases of ureteral calculi in house patients showed that 55.4 per cent had some type of manipulation before the stone passed. Some type of ureterolithotomy was done in 37.5 per cent of which 15.2 per cent were lumbar. A nephrectomy was performed in 2.3 per cent. No treatment was attempted in 4.8 per cent.

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[2] Dees, J. E.: South. Med. J., **39**: 208, 1946.
[3] Prince, C. L.: J. Urol., **54**: 368, 1945.
[4] Barelare, B.: J. Urol., **65**: 980, 1951.

The following factors should be taken into consideration before determining whether to manipulate a stone from the upper ureter or to remove it surgically: 1) The length of time the stone has been present is much more important than the size of the stone; 2) whether the patient accepts or resents pain and cystoscopic procedures; 3) the degree of infection present, and fourth, the ability of the operator to remove successfully calculi by instrumentation. This is a personal factor that each of us has to evaluate. We believe that calculi should be removed surgically from the upper ureter when you doubt that it will pass readily into the lower ureter, and when you anticipate difficulty in removing it from the lower ureter instrumentally. You will relieve many patients of pain and subsequent morbidity as well as late sequellae due to manipulation by a lumbar ureterolithotomy. It is a simple, definitive operation that should be used frequently.

SUMMARY

It has been our purpose to emphasize the immediate and the late hazards of instrumental removal of ureteral calculi, and to emphasize the safety and simplicity of removing a calculus while in the upper ureter through a muscle splitting lumbar incision.

This procedure has been employed in 44 cases without surgical complications. In 4 cases it was necessary to increase the incision by cutting the muscles. In 6 cases the latissimus dorsi muscle was intentionally cut and the remaining structures separated.

The absence of trauma to the ureter, immediate or late complications, the short hospital stay, and the positive removal of the calculi make it a procedure which should be used frequently.

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HYPERCHLOREMIC ACIDOSIS OF URETEROSIGMOIDOSTOMIES

A. D. MITCHELL AND WILLIAM L. VALK

From Department of Surgery, Urology Section, University of Kansas Medical Center, Kansas City, Kansas

Diversion of urine to the bowel is too valuable a procedure to be abandoned because of a resulting abnormality in the patient's body chemistry. For all patients with exstrophy of the bladder and many with carcinoma of the bladder we believe that this procedure is essential.

Since the report of Ferris and Odel[1] on this subject in 1950, much thought has been devoted to the problem and many questions have arisen.

The objectives of this study have been to determine the relative roles of the kidney and rectosigmoid colon in producing hyperchloremic acidosis and the development of a practical and effective therapeutic regimen for its management.

With urinary diversion to the rectosigmoid and intermittent rectal emptying, our conclusions are that sodium chloride[2, 3] and ammonium chloride are reabsorbed in varying amounts, depending on the serum level of chloride and the concentration of these electrolytes in rectal urine. Reabsorption of sodium chloride as such allows for an excess of chlorine, for the plasma ratio of sodium to chlorine is normally 1:.7 while reabsorption of sodium chloride is 1:1.[4] Thus if 100 milliequivalents of sodium chloride are reabsorbed, there is an excess of 30 milliequivalents chlorine in plasma without cation coverage. Reabsorption of ammonium chloride leads to conversion of ammonia to urea by the liver[5] causing elevation of the blood urea nitrogen and nonprotein nitrogen and necessitating that chlorine displace an equivalent amount of the bicarbonate radical in combination with base. Thus reabsorption of 100 milliequivalents ammonium chloride results in 100 millequivalents of chlorine in plasma to displace 100 millequivalents bicarbonate radical from sodium. There is, therefore, no true loss of sodium and potassium but a relative deficit of sodium as compared to a true loss of the bicarbonate radical. Intracellular potassium may be drawn into the extracellular space to make up part of this deficit of sodium.

Plasma bicarbonate is lowered by carbon dioxide loss in the lungs. The deficit of bicarbonate radical in the glomerular filtrate necessitates a moderate increase in proximal tubular reabsorption of chlorine with sodium to keep the anion pattern fairly constant. All the filtered bicarbonate radical is reabsorbed in the proximal tubule and none reaches the distal tubule. This distal tubular bicarbonate radical deficit is the stimulus necessary for increased hydrogen ion exchange and ammonia production. In an effort to compensate for this acidosis, the distal tubular apparatus elaborates more ammonia to excrete with the excess acids and thus a vicious cycle is established (fig. 1). This may equilibrate

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Read at annual meeting, South Central Section, American Urological Association, Houston, Texas, October 20, 1951.

[1] Ferris, D. O. and Odel, H. M.: J.A.M.A., **142:** 634, 1950.

[2] Goldschmidt, S. and Dayton, A. B.: Am. J. Physiol., **48:** 419, 1919.

[3] Goldschmidt, S.: Physiol. Rev., **1:** 421, 1921.

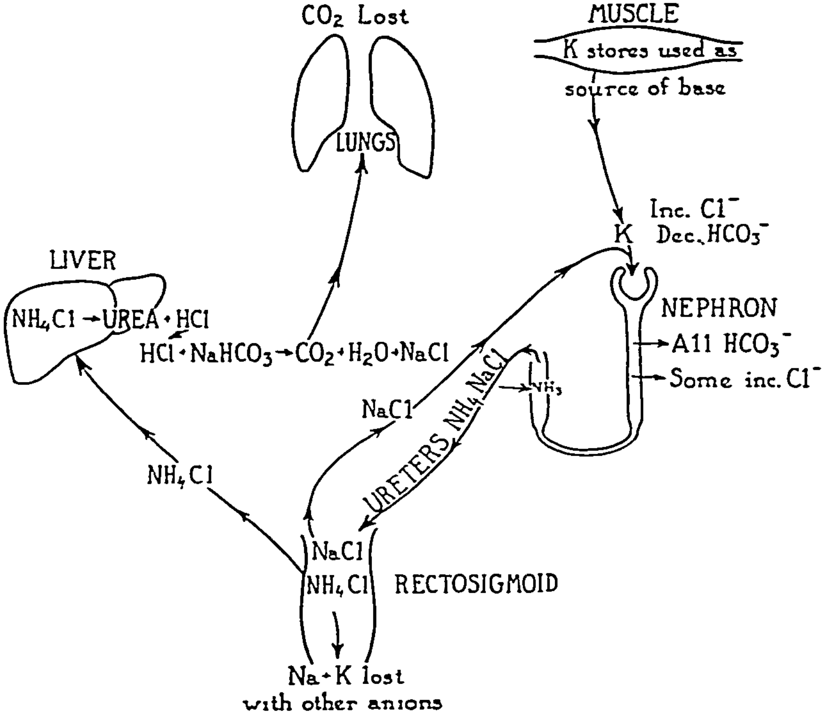
[4] Foster, F. P., Drew, D. W. and Wiss, E. J.: The Lahey Clinic Bull., **6:** 231, 1950.

[5] Sprinson, D. B. and Rittenberg, D.: J. Biol. Chem., **180:** 707, 1949.

when the serum chloride reaches a certain elevation and the concentration of the urine is lowered by increased fluid intake.

The clinical picture of such patients has been adequately described in many reports.[1, 4, 6, 7] Anorexia, nausea, vomiting, dehydration, abnormal tastes in the mouth, and even states of coma may develop if the abnormality is not corrected soon enough.

Goldschmidt and Dayton showed in 1919[2] that dogs demonstrate two-way permeability of the colon to electrolytes. With a normal serum chloride level, dogs lose chloride into the colon at concentrations of sodium chloride in the colonic fluid below 27.4 milliequivalents per liter. Above this concentration in the colonic fluid sodium chloride is absorbed into the blood in increasing amounts as the colonic concentration increases. Further, with an elevated blood sodium chloride level, chlorides may pass into the colon at colonic chloride concentrations of 37 milliequivalents per liter. This emphasizes the importance of a high urinary output in patients with ureterosigmoidostomies.


CO_2 Lost
MUSCLE
K stores used as source of base
LUNGS
Inc. Cl^-
K Dec. HCO_3^-
LIVER
$NH_4Cl \rightarrow$ UREA + HCl
$HCl + NaHCO_3 \rightarrow CO_2 + H_2O + NaCl$
NEPHRON
$\rightarrow$ All HCO_3^-
$\rightarrow$ Some inc. Cl^-
NH_3
NaCl
URETERS NH_4 NaCl
NH_4Cl
NaCl
NH_4Cl
RECTOSIGMOID
Na + K lost
with other anions

Hyperchloremic Acidosis of Ureterosigmoidostomies

FIG 1

That patients with uretosigmoid transplants reabsorb these electrolytes from the rectosigmoid is shown by figure 2. Twenty-four-hour urine specimens were

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[6] Kekwick, A., Paulley, J. W., Riches, E. W. and Semple, R. Brit. J. Urol., 23: 112, 1951.
[7] Rosenberg, M. L. and Elliot, J. S. Stanford Med. Bull., 9: 13, 1951.

collected on consecutive days both while in a state of hyperchloremic acidosis and after correction of acidosis. Dietary intake was constant for the consecutive studies. It can be seen that the quantities of chloride and ammonia recovered by tube were greater than those recovered by intermittent voiding. The concentration of chloride in rectal urine was very high in the tube specimens collected during acidosis but was under 27 milliequivalents per liter after correction of acidosis. In patient G. H. the amount of sodium recovered by rectal tube was also higher than the pan-voided urine. The quantity of ammonia recovered is higher than would be expected and probably some of this ammonia is due to bacterial decomposition of urea. However, if bacterial decomposition played a significant role the pan-voided specimens should contain more ammonia than the tube specimens. Urine specimens were collected for short periods under toluene and ammonia was determined immediately after collection with high values to confirm high ammonia excretion by these subjects.

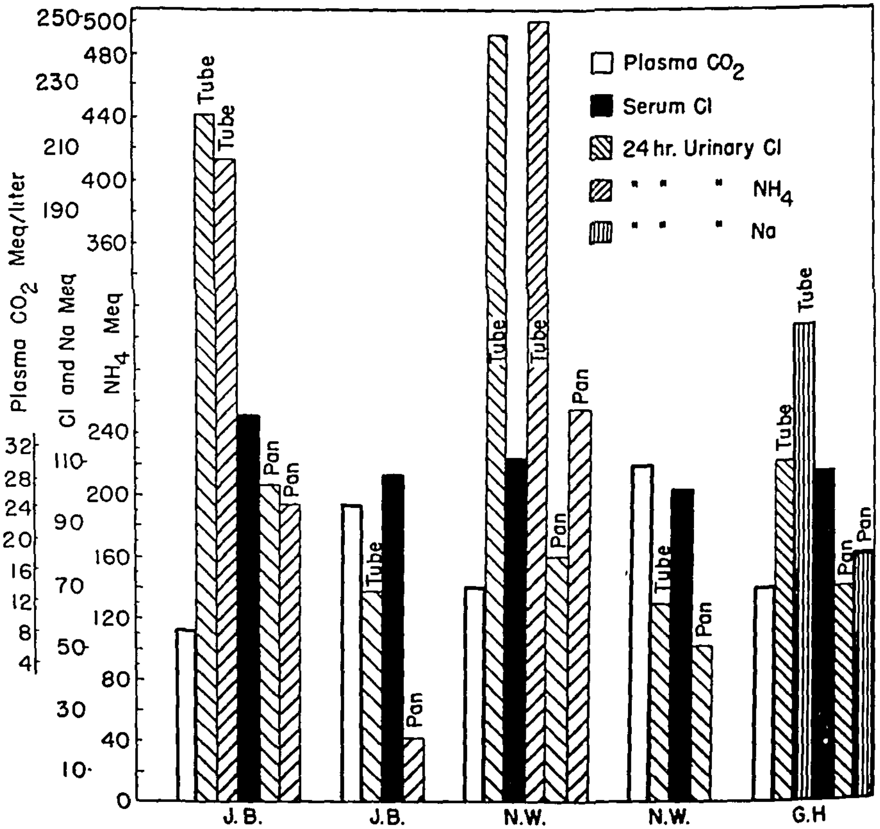

FIG. 2

That such reabsorption occurs is further demonstrated by case reports of hyperchloremic acidosis of ureterosigmoidostomies being corrected by rectal tube drainage and lavage of the rectum with tap water.[1]

All patients with ureterosigmoidostomies may potentially develop this electrolyte derangement. Ferris and Odel[1] report that of 112 patients with ureterosigmoidostomies, 79 per cent had an elevation of serum chlorine and 80 per cent had depression of the plasma bicarbonate. The reason some did not develop hyperchloremia must have been because of low chloride and high fluid intake so that the concentration of chlorine in the colonic urine was not high enough for reabsorption. In addition, these patients probably emptied their bowels fairly often. We have not seen a patient yet with ureteral transplants to the colon whose lack of hyperchloremia could not be explained in this manner.

TEMPORAL ASPECTS

As soon as the rectal tube is removed after ureterosigmoidostomy, reabsorption of electrolytes begins unless the patient has a low chloride intake and a large fluid intake. In some instances these requirements prevail until the patient leaves the hospital, after which time he may increase his chlorine intake and decrease his fluid intake and return to the hospital in a few weeks or months with hyperchloremic acidosis.

Ferris and Odel's first patient had a serum chlorine of 112 milliequivalents per liter by the twenty-second postoperative day. Their second patient reported had a normal serum chlorine (104 milliequivalents per liter) and carbon dioxide combining power (23 milliequivalents per liter) for 21 days after operation during which time he was rectally incontinent. Seven days after this patient became rectally continent his serum chlorine was 109 milliequivalents per liter and the carbon dioxide combining power was 19 milliequivalents per liter.

One of our patients, R. E. O., did not show any chemical abnormality while hospitalized and properly managed but returned 5 weeks after dismissal and 3½ months after operation with severe hyperchloremic acidosis. D. S. B., No. 51-121, had a serum chlorine of 123 milliequivalents per liter and a carbon dioxide of 10.1 milliequivalents per liter 23 days after ureterosigmoidostomy. B. S. D., No. 50-8009, had a serum chlorine of 109 milliequivalents per liter and a carbon dioxide combining power of 12.4 milliequivalents per liter 15 days after transplants and 11 days after removal of the rectal tube.

It is reported that this condition may disappear in 6 months[4, 8] and that the low salt regimen may be discontinued. However, Ferris and Odel report a case 9 years after operation and we have had 4 cases over 2 years since operation in which the patients exhibited this phenomenon. Harvard and Thompson[9] in reporting late results of uretero-intestinal anastomoses present 1 case 35 years after transplants with a blood urea nitrogen of 74 mg. per cent and a creatinine of 1.8 mg. per cent. They stated that this patient's serum chlorine level was normal but the great disparity between blood urea nitrogen and creatinine suggests reabsorption persisting at this late date.

Patients who do not exhibit hyperchloremic acidosis after 6 to 12 months have compensated by the same three measures that prevent this abnormality

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[8] Flocks, R. H.: J.A.M.A., 139: 626 1949.

[9] Harvard, B. M. and Thompson, G. J.: J. Urol., 65: 223, 1951.

from developing in some patients in the first place, namely: 1) low chloride intake, 2) high fluid intake and 3) frequent emptying of the bowel. There is no change in the inherent potentiality of such patients to develop hyperchloremic acidosis at any time after operation.

RENAL ASPECTS

In our opinion this type of acidosis can develop in the presence of good renal function. The kidneys respond to an increased load of chlorine and decreased load of the bicarbonate radical in the same manner they do to experimental orally ingested ammonium chloride acidosis.

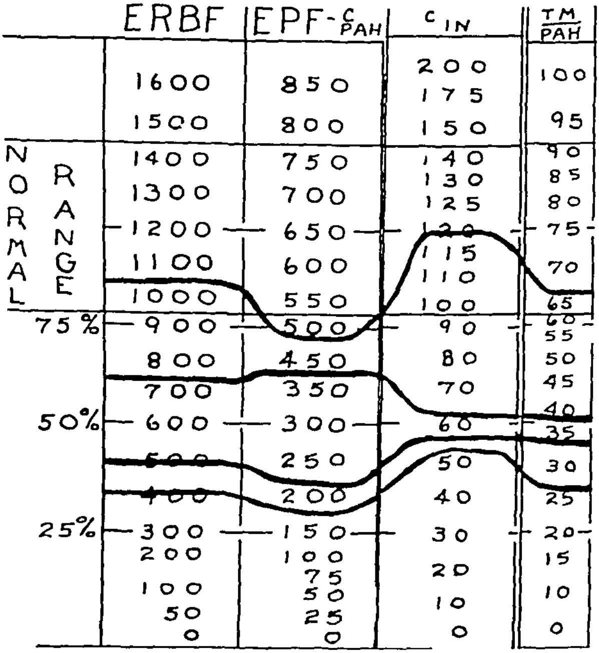

FIG. 3. ERBF = effective renal blood flow in cc/min. EPF = effective renal plasma flow in cc/min. C_{PAH} = para-amino hippurate clearance. C_{IN} = inulin clearance in cc/min. TM_{PAH} = tubular mass for para-amino hippurate mg./min.

Measurement of effective renal blood flow, glomerular filtration rate and tubular mass for para-amino hippurate in our patients with hyperchloremic acidosis produced values at or above 35 per cent of normal, which is the usually accepted minimum amount of function required to maintain health.[10] The patient with the best function had as severe a degree of acidosis as the other patients (fig. 3).

If disturbed renal function were at fault in this syndrome, which it is not, the proximal tubule could theoretically fail to reabsorb the bicarbonate radical, in which event an increased amount of chlorine would be reabsorbed to keep the total anion pattern constant and the bicarbonate radical would be lost in the urine. This cannot be the case because an excess of bicarbonate radical in distal tubular urine would prevent ammonia production and we know these patients elaborate normal quantities of ammonia. This very fact of increased ammonia production likewise eliminates disturbed distal tubular function as the cause.

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[10] Drury, D. R.: J. Urol., 41: 111, 1939.

Kekwick,[6] in discussing this problem, cites the papers of Greenspan,[11] Peterman[12] and Baines[13] on the rare renal tubular disease causing hyperchloremic acidosis in patients with an intact urinary tract. Since the papers of Latner[14] and Govan[15] this uncommon but definite clinical syndrome appears to be a failure of proximal tubular reabsorption of the bicarbonate radical rather than a pure lower nephron or distal tubular disease as was formerly thought. Pitts[16] has shown that the sum of chlorine and the bicarbonate radical reabsorbed in the proximal tubule is constant and therefore failure to reabsorb the bicarbonate radical leads to increased reabsorption of chlorine and increased delivery of the bicarbonate radical to the distal tubule which prevents ammonia production. This subject is discussed to show that patients who have undergone ureterosigmoidostomy do not have the same disease. Patients with hyperchloremic acidosis who have been subjected to ureterosigmoidostomy excrete normal amounts of chlorine into the rectum and therefore cannot be reabsorbing excessive chlorine in the proximal tubule. They also excrete normal amounts of ammonia and therefore cannot have an excess of the bicarbonate radical being delivered to the distal tubule.

Sartorius Roemmelt, and Pitts,[17] in an excellent study of ammonium chloride acidosis in man, have demonstrated much the same picture that patients with acidosis of ureterosigmoidostomy demonstrate. There was elevation of serum chlorine, depression of plasma bicarbonate and increased renal excretion of ammonia.

That reabsorbed or ingested ammonia is converted to urea by the liver and is not excreted as ammonia by the kidney has been shown by Sprinson and Rittenberg[5] in isotope studies, and that glutamine is the substrate for urinary ammonia has been shown by Van Slyke.[18]

Reabsorption of ammonia in the patients under consideration and not the reabsorption of urea explains the elevation of the blood urea nitrogen and nonprotein nitrogen with a normal creatinine level. Proof of this is given (table 1) by cases of ours whose nonprotein nitrogen reverted to normal with correction of acidosis but without rectal tube drainage. Correction of acidosis reduces renal formation of ammonia, and there is thus less ammonium chloride in colonic urine for reabsorption while the same amount of urea is present both in and out of acidosis.

[11] Greenspan, E. M. Arch Int. Med., **83:** 271, 1949.
[12] Peterman, M. G.: Am. J. Dis. Child., **69:** 291, 1945.
[13] Baines, G. H., Barclay, J. A. and Cooke, W. T.: Quart. J. Med., **14** (n.s.): 113, 1945.
[14] Latner, A. L. and Burnard, E. D.: Quart. J. Med., **19** (n.s.): 285, 1950.
[15] Govan, A. D. Telford: Quart. J. Med., **19** (n.s.)· 277, 1950.
[16] Pitts, R. F., Ager, J. L. and Schiess, W. A.: J. Clin. Invest., **28:** 35, 1949.
[17] Sartorius, O. W., Roemmelt, J. C. and Pitts, R. F.: J. Clin. Invest., **28:** 423, 1949.
[18] Van Slyke, D. D., et al.: J. Biol. Chem., **150:** 481, 1943.

That patients with hyperchloremic acidosis who have undergone ureterosigmoidostomy have an obligatory polyuria has been stated.[6] That such patients lose an excess of water is a fact, and they are easy victims of dehydration. However, if the distal tubule can elaborate a normal amount of ammonia in response to acidosis it is logical to assume that it will be able to retain water in response to dehydration. Therefore, we presume that a large part of the obligatory water loss is due to diffusion of water into the bowel containing a concentrated solution of urine. There is thus a dual mechanism of water loss. Sartorius et al.[17] state that in ammonium chloride acidosis the loss of fixed base is accompanied by the excretion of nearly equivalent quantities of water; this would explain the renal loss of excess water. That concentrated solutions of electrolytes will draw fluid into the colon is well established,[3] thus explaining the colonic role in this loss of fluid.

TABLE 1

	Cl	CO_2	NPN	Cr
G. H.	123	18.1	75	
	89	21.8	33	
	106	15.4	54	
C. G.	116	19.5	48.5	1.3
	100	23.5	34	1.5
S. B.	129	17.8	70	2.0
	106	23.2	37.5	1.2
J. B.		11.8	86	
		20.3	30	
	125	5.0	84	1.5
	98	32.2	34	
	125	13.5	54	2.2
	103	27.0	45	
B. O.	115	8.5	50	1.2
R. O.	120	12.7	53.8	1.9
	96	26.1	35.0	1.45

Cl = serum chloride millequivalents per liter.
CO_2 = carbon dioxide combining power millequivalents per liter.
NPN = nonprotein nitrogen milligrams per cent.
Cr = creatinine milligrams per cent.

TREATMENT

In light of the preceding discussion treatment may be outlined as follows: The earliest opportunity to do anything about hyperchloremic acidosis is at the time of operation. Boyce[19] has shown that in dogs, diversion of the urine to the cecum is uniformly fatal and that the lower in the rectum the urinary tract can be diverted the less urine will reflux into the more absorptive upper sigmoid colon. Therefore, our first step in treatment is to transplant the ureters as low in the rectosigmoid as is surgically feasible.

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[19] Boyce, W. H.: J. Urol., 65: 241, 1951.

In the immediate postoperative period with a rectal tube in place the patient's fluid and electrolyte requirements are not influenced by colonic reabsorption.

When the rectal tube is removed, a prophylactic regimen should be instituted immediately. First, the patient should develop a fluid intake of 4500 to 5000 cc daily to keep the electrolyte concentration of rectal urine dilute and to foster the second requirement which is emptying of the rectum every 1 to 1½ hours. Lastly a diet low in chlorides* should be required, and the sodium which is thereby eliminated from the diet should be replaced with small amounts of sodium bicarbonate. Usually 1 to 4 gm. of sodium bicarbonate (12–48 milliequivalents) will be adequate, but each case must be individualized. If this program is followed most cases will need no further restrictions.

It must always be borne in mind that these patients can become suddenly and seriously ill by what would be rather mild dehydration in a patient with an intact urinary tract.

Periodic postoperative follow-up studies should include serum chloride, carbon dioxide combining power, nonprotein nitrogen and creatinine. The amount of sodium bicarbonate required will depend on the individual response. If it is not convenient to obtain chloride and carbon dioxide determinations, the nonprotein nitrogen and creatinine will be valuable. If both nonprotein nitrogen and creatinine are normal the patient is probably not in acidosis. If the nonprotein nitrogen is elevated and the creatinine is normal, serum chloride and carbon dioxide determinations should be obtained. If both nonprotein nitrogen and creatinine are elevated the patient has renal failure.

For severe hyperchloremic acidosis with anemia and perhaps coma, prompt and adequate treatment of dehydration plus constant rectal drainage are indicated. Glucose in water and sodium lactate solution should be given intravenously in rather large quantities; about 5000 cc the first day, to correct both the actual fluid and relative sodium deficits. Usually within 24 to 48 hours the patient can take fluids by mouth, but before the rectal tube is removed the program outlined at the outset of treatment should be started. Rosenberg and Elliot[10] emphasize the importance of a low serum potassium in such patients and recommend the use of potassium in treatment. Sartorius et al.[17] have shown that in ammonium chloride acidosis much of the base which is lost in neutralizing urinary acids is potassium drawn from the intracellular compartment. In their studies the plasma level of potassium did not reflect the great loss of potassium from these stores, and we, therefore, cannot use plasma potassum concentration as the index for replacement. In the acutely ill patient potassium citrate may be given in amounts of 3 gm. daily until acidosis is corrected. However, again it should be mentioned that this type of acidosis is not due to a deficit of cations but to a disproportion of chloride and the bicarbonate radical; the total cations and anions remain normal or slightly elevated.

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* The low chlorine diet differs from a low salt diet primarily by eliminating foods containing potassium chloride. Patients may use a salt substitute without consulting their physician and this is, of course, worse than salt because they get chlorine with no sodium.

For patients uncontrolled at home by the aforementioned measures, we have used exchange resins rectally without success. Dock and Frank,[20] in discussing the use of cation exchangers, showed that such patients lose a great amount of base leading to high serum chloride, low plasma bicarbonate and increased excretion of ammonia in the urine. Rosenberg and Elliot[10] suggested use of anion exchangers by mouth to correct hyperchloremic acidosis of ureterosigmoidostomy.

Anion exchangers presently available will only bind chloride at a fairly low pH and were they used by mouth they would lose chlorides bound in the stomach upon reaching the alkaline medium of the intestine.[21, 22] Our initial study has been with an anion exchanger SKF 1713.* Each gram of this resin in vitro will bind 10 meq of chloride. The selectivity of this resin is as follows: OH^-, $PO_4^{\equiv}$, $SO_4^{=}$ Cl^-, reading from left to right with a decreasing exchange potential. With acidosis and increased excretion of ammonia, rectal urinary pH has averaged 8.5 in our patients. At pH 6 this resin will efficiently bind Cl^-, but at pH 7 a good portion of the anions will be eluted from resin.[22]

Use of both hydrogen exchange resin† and anion exchange resin in vivo has not been effective because of the tendency to act as a buffer system. The pH of freshly voided urine is reduced from 8.4 to 6.2 within 15 minutes after mixing with anion and hydrogen resins and after 48 hours is 6.7. These results have not been obtained from use of resins per rectum, which we have not yet explained.

CASE REPORTS

D. S. B., No. 51-122, a white female child, was admitted at 3 months of age with exstrophic bladder and normal upper urinary tract. Bilateral Coffey 1 ureterosigmoidostomies had been performed; the postoperative course was uneventful both subjectively and objectively. One month later she had hyperchloremic acidosis. History revealed poor fluid intake and rectal emptying about every hour or two. At age of 12 months the patient had undergone cystectomy at which time excretory urograms revealed normal function and architecture.

As can be seen from table 2, after institution of a low chloride intake and constant maintenance of a large fluid intake, the electrolyte problem was solved. Her fluid intake averaged 110 cc per kilogram body weight and although her mother changed her diaper about every 2 hours, observation revealed that she extruded small amounts of urine every 5–10 minutes. Thus the 3 requirements of 1) low chloride intake, 2) large fluid intake and 3) frequent rectal emptying are fulfilled. When rectal continence develops, the child may again have hyperchloremia and will be carefully followed in this regard.

S. G., No. 147840, a white male child, had Coffey 1 ureterosigmoidostomies performed on October 24, 1947, at 1 year of age, and cystectomy performed on

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[20] Dock, Wm. and Frank, N. F.: Am. Ht. J., **40:** 638, 1950.

[21] Wheaton, R. M. and Bauman, W. C.: Ind. and Eng. Chem., **43:** 1088, 1951.

[22] Heming, A. E.: Personal communication.

* Furnished by A. E. Heming; Smith, Kline & French Laboratories, Philadelphia.

† Furnished by Wm. M. Swain, Director of Clinical Research, The National Drug Company.

March 11, 1948, for exstrophy of the bladder. Excretory urograms made annually since operation have been normal.

On August 24, 1951, forty-six months postoperative, his parents felt that growth and development were normal compared to his siblings. His fluid intake was greater than his siblings or parents, and he asked for more fluids than were given. He emptied his rectum at least every hour and was incontinent at night.

Laboratory work revealed: serum chloride 104 milliequivalents per liter, carbon dioxide combining power 19.9 milliequivalents per liter, nonprotein nitrogen 39 mg. per cent, creatinine 1.0 mg. per cent. Accurately measured fluid balance revealed 2500 cc intake and 1500 cc urine which is large for a child this age. Instructions for a large fluid intake and regular diet without salt were given.

TABLE 2

	Cl	Na	K	CO_2	NPN	Cr
10-26-50	Ureterosigmoidostomies					
11-18-50	123			10.2		
	Adequate fluids and alkali					
12-19-50	108			21.2		
	Home					
1-6-51	129			17.8	130	
	Low Cl diet					
1-12-51	110				41	1 5
5-21-51	100	142		18.5		
7-24-51	102	137	5.6	21.2	37.5	1.2

Cl = serum chloride.
Na = sodium.
K = potassium
CO_2 = carbon dioxide combining power in millequivalents per liter.
NPN = nonprotein nitrogen in milligrams per cent.
Cr = creatinine in milligrams per cent.

It is believed that this child controlled his chloride problem by a large fluid intake which kept the urinary chlorides dilute and also necessitated frequent rectal emptying. By reducing his chloride intake somewhat the carbon dioxide combining power should be elevated.

R. E. O., a white male 56 years old, had carcinoma of the bladder. Coffey 1 ureterosigmoid anastomoses were performed January 26, 1951, and total cystectomy March 3, 1951. During the operative interval he had no electrolyte disturbance and had a rectal tube in place for 7 days after cystectomy. He was dismissed in March 1951, with instructions concerning fluid intake and a low chlorine diet.

He returned on May 4, 1951 with a serum chlorine of 136 milliequivalents per liter. Parenteral alkali, fluids, restricted chloride intake and rectal tube drainage resulted in a serum chlorine of 106.8 milliequivalents per liter and carbon dioxide combining power of 23 milliequivalents per liter on May 18, 1951. He was again instructed in the low chlorine diet, large fluid intake and frequent rectal emptying and was placed on 48 milliequivalents (4 gm.) of soda bicarbonate.

He returned July 30, 1951, complaining of nausea, vomiting, anorexia, and a metallic taste in his mouth. At that time laboratory work showed: nonprotein nitrogen 53.8, creatinine 1.9, serum chlorine 120.6 milliequivalents per liter, carbon dioxide combining power 12.7 milliequivalents per liter. He was given 3000 cc 1/6 M lactate intravenously, a low chlorine diet, 96 milliequivalents sodium bicarbonate daily, rectal tube drainage and forced fluids by mouth. On August 2 laboratory results were: serum chlorine 95 milliequivalents per liter and carbon dioxide combining power 24.6 milliequivalents per liter. He had regained his appetite and felt quite normal. The metallic taste lasted until August 4, 1951. He was then dismissed on the same program plus 96 milliequivalents sodium bicarbonate daily for 1 week and then 48 milliequivalents sodium bicarbonate daily. His history revealed that he had added liberal daily amounts of salted peanuts to his diet. On August 27, he was in good health with a serum chlorine of 96 milliequivalents, carbon dioxide combining power 26.1 milliequivalents per liter, nonprotein nitrogen 35, creatinine 1.45. His urine collected by tube contained 24.14 milliequivalents chlorine per liter and 2.86 meq ammonium per liter. Excretory urograms show excellent function and normal architecture.

TABLE 3

	Cl	Na	K	CO_2	NPN	Cr
4-13-51	111	133		14	49	1.8
Low Cl—$NaHCO_3$ 6 gms/day						
4-23-51	101	140	3.8	29		
6-27-51	106	140		20.7		
8-4-51	102			27.5		
10-20-51	103			25.2	30.9	1.5

Cl = serum chloride in millequivalents per liter.
Na = sodium in millequivalents per liter.
K = potassium in millequivalents per liter.
CO_2 = carbon dioxide combining power in millequivalents per liter.
NPN = nonprotein nitrogen in milligrams per cent.
Cr = creatinine in milligrams per cent.

N. W., No. 49-4173, a 35-year-old white man with carcinoma of bladder, underwent Coffey 1 ureterosigmoidostomies and total cystectomy on July 27, 1949. On reviewing his immediate postoperative records, he had a moderate degree of hyperchloremic acidosis which went unrecognized and untreated.

He was seen in April 1951, complaining of feeling "run down," with anorexia and some weight loss. Reference to table 3 shows the degree of hyperchloremic acidosis present. The difference between tube collected and voided urines shows how much reabsorption he had. (fig. 2, N.W.) After correction of acidosis by low chlorine diet and alkali the excretion of chlorine dropped remarkably on both the tube and pan specimens and the negligible difference shows that the large fluid output kept the chlorine dilute enough to prevent much reabsorption.

Renal function studies showed normal C_{In}, about 80 per cent normal renal blood flow and 87 per cent normal TM_{PAH}.

He was dismissed on a low chlorine diet, large fluid intake and 72 milliequivalents (6 gm.) sodium bicarbonate daily. His electrolyte pattern is normal 6 months later and he is subjectively and objectively well.

J. B., No. 50-7294, a 68-year-old white man, had papillomatosis of the bladder in 1944 and in July 1949, bilateral hydro-ureters were developing as a result of a small contracted bladder. Bilateral ureterosigmoidostomies were done by the Nesbit elliptical technique.[23] An intestinal fistula developed with constant loss of urine through the fistula for 7 months, during which time he had no electrolyte disturbance.

TABLE 4

	SERUM		K	CO_2	NPN	Cr	TREATMENT
	Cl	Na					
Hospital							
10-15-50	121			5	84	1.5	Soda 3 gm.
Hospital							
4-4-51	118	144	5.8	14.4			
4-7-51	106			24.4			
4-13-51	103	137		27	45		
Out Patient							
4-23-51	116	138		10.1			
							Soda 10 gm.
5-28-51	108			22.7	46		
							Edema
6-25-51	112			16.8			Soda 3 gm.
Hospital							
7-30-51	111			11.9			Anion Resin 45 gm.
							Soda 3 gm.
8-6-51	103			23.2			
Out Patient							
8-20-51	109			13.6	56		
8-27-51	104			16.4	50	1.8	Anion resin 45 gm.
							Cation resin 25 gm.
10-1-51							Anion resin and hydrogen resin
10-6-51	106			20.7	41	1.7	

Cl = serum chloride in millequivalents per liter
Na = sodium in millequivalents per liter.
K = potassium in millequivalents per liter.
CO_2 = carbon dioxide combining power in millequivalents per liter.
NPN = nonprotein nitrogen in milligrams per cent.
Cr = creatinine in milligrams per cent.

Table 4 and figure 4 show his recurrent hyperchloremic acidosis which was easily corrected by strict dietary management in the hospital, but was poorly controlled at home.

Renal function studies showed: glomerular filtration rate 58.4 cc/min (48.7

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[23] Nesbit, R. M.: J. Urol., 61: 728, 1949.

per cent normal inulin clearance); effective renal plasma flow 227 cc/min (35 per cent normal PAH clearance); effective renal blood flow 490 cc/min (39 per cent normal); tubular mass for PAH 34.6 mg/min (46 per cent normal $\mathrm{TM}_{\mathrm{PAH}}$). See figure 3. All liver function studies were normal.

The improvement with use of combined hydrogen and anion exchange resins is felt to be coincident with proper electrolyte intake rather than to the resins since examination of rectal urine showed no significant electrolyte binding.

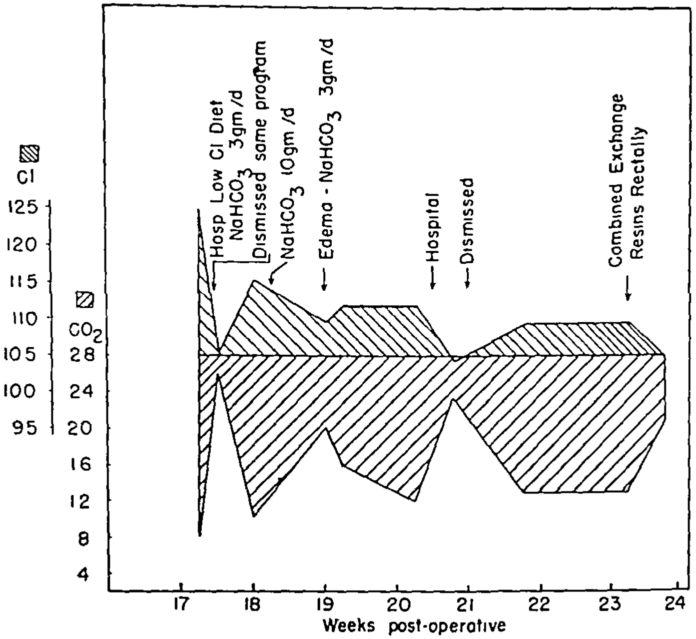

FIG. 4

CONCLUSIONS

All humans reabsorb Cl, Na, and NH_3 from the rectum in a fairly uniform manner.

All patients with urinary diversion to the sigmoid colon have the potentialities of developing hyperchloremic acidosis.

There is no lag period in the development of this potentiality and as long as urine is diverted to the rectosigmoid the potentiality will remain.

The development and degree of hyperchloremic acidosis do not depend upon the level of renal function or abnormal distal tubular function.

The nonprotein nitrogen and blood urea nitrogen are elevated because of reabsorption of ammonia and its conversion to urea by the liver and not because of reabsorption of urea from rectal urine.

The type of uretero-intestinal anastomosis performed does not influence the development of hyperchloremic acidosis but the location of anastomosis does.

Proper management of patients with uretero-intestinal anastomosis must include: a) low chloride intake, b) large (4500–5000 cc) fluid intake, c) frequent

(1–1½) emptying of rectum, d) supplementary sodium, usually 12–60 meq/day as $NaHCO_3$ (1–4 gm.).

A combination of hydrogen and cation exchange resins for rectal use has been unsuccessful to date in removing electrolytes from rectal urine.

SUMMARY

The physiology of hyperchloremic acidosis of ureterosigmoid anastomoses is discussed. A rational program of management is outlined. Representative cases are presented.

ADDENDUM

Since presentation of this paper in October 1951, the excellent work of Lapides[24] on this subject has been studied. His conclusion is that hyperchloremic acidosis of ureterosigmoidostomies results from a dual mechanism, with renal tubular damage as the determinative factor and intestinal absorption playing a secondary role.

We cannot entirely reconcile our findings with Lapides. We have one patient with ureteral transplants who has 30 per cent normal glomerular filtration, 20 per cent normal effective renal blood flow and 25 per cent normal TM_{PAH} whose blood urea and creatinine are elevated and yet who has no hyperchloremia. Her fluid intake is high and chloride intake is low.

Of the patients examined with renal function studies only one was done while the patient was actually acidotic which may be one defect in our study. However, if renal tubular damage is determinative then all but the highest patient listed in Fig. 3 should have been difficult, if not impossible, to control by diet.

Lapides' paper should be read by anyone interested in this subject.

[24] Lapides, Jack: Surg., Gynec & Obst., 93: 691, 1951.

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PRELIMINARY REPORT: A STUDY OF THE EFFECTS OF BANTHINE ON THE HUMAN BLADDER

JACK LAPIDES AND AUSTIN DODSON, JR.

From the Department of Surgery, University of Michigan Medical School, Ann Arbor, Mich.

In 1947 Nesbit and co-workers[1] reported the effects of the tetraethyl ammonium ion, a quarternary ammonium salt, on the urinary bladder. They found that the drug produced paralysis of the bladder by impairing the transmission of nerve impulses through the autonomic ganglia. Tetraethyl ammonium chloride was not used therapeutically in bladder disorders because of its severe side-effects and also because it was not effective when administered orally. Recently Robinson and Cusic[2] prepared a new quarternary ammonium derivative, B-diethylaminoethyl xanthine-9-carboxylate methobromide, which has been commercially designated as Banthine. Animal experimentation with this drug[3] demonstrates that, in small amounts, it inhibits structures innervated by postganglionic cholinergic nerves and blocks the action of injected acetylcholine upon these structures; in somewhat larger doses it blocks transmission through the autonomic ganglia; and, in lethal concentrations, it has a curariform effect. Workers[4, 5, 6] investigating the effects of Banthine on peptic ulcers in patients have observed the occurrence of acute urinary retention in several males with benign prostatic hypertrophy who received the drug orally.

In view of the action of Banthine in blocking impulses transmitted through the parasympathetic nerves, its relatively low toxicity and its effectiveness when administered orally, it was decided to investigate its effect upon normal and abnormally functioning urinary bladders in an effort to establish its position in the therapeusis of neurogenic bladder disorders.

METHODS

Cystometric examination was employed in determining the effects of Banthine upon the bladder. The drug was administered both orally and intravenously to human subjects. A cystometric determination was obtained prior to drug administration. If Banthine was given intravenously, then a repeat cystometric determination was performed within ten minutes after injection. If the oral preparation was used, then the cystometric determination was made 3–5 days

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[1] Nesbit, R M , Lapides, J , Valk, W W , Sutler, M , Berry, R L , Lyons, R H , Campbell, K N and Moe, G K J Urol , **57:** 242–250, 1947.

[2] Cusic, J W and Robinson, R A Presented before the Medicinal Division at the meeting of the American Chemical Society, Philadelphia, April 9–13, 1950

[3] Hambourger, W E , Cook, D L , Winburg, M M and Freese, H B J Pharmacol. and Exper Therap , **99:** 245–254, 1950

[4] Grimson, K Gastroenterology, **14:** 583–586, 1950

[5] BROWN, C H and Collins, E N Clev Clin Quart , **17:** 234–241, 1950

[6] Kern, F , Jr , Almy, T P and Stolk, N J Gastroenterology, **17:** 198–208, 1951.

Banthine supplied by G D Searle and Company

Aided by a research grant from G D Searle and Company.

Additional effects and therapeutic uses of Banthine in urinary tract abnormalities are being investigated, results will be published when experimental data permit definite conclusions after the start of therapy. The intravenous dosage varied from 100–150 mg. while the oral dose varied from 25–100 mg. four times a day. In some of the patients receiving oral Banthine, the drug was stopped and then after 5 days another cystometric examination was made. A standardized method[1] was employed in performing the cystometric determinations. Observations were made on normal bladders, uninhibited neurogenic bladders and reflex neurogenic bladders.

RESULTS

A. *Normal bladders.* Four patients composed this series. Two of the subjects received intravenous doses of 150 mg. and two 100 mg. of Banthine. In no patient was bladder tonus, capacity or sensation affected. The two patients who received 150 mg. intravenously had complete urinary retention 15 minutes after Banthine administration. No bladder effect was noted in one patient who received 100 mg. intravenously while the other patient developed partial urinary retention. Figure 1 demonstrates the pre- and post-Banthine cystometric determinations in a patient who received 150 mg. intravenously. Figure 1, A the pre-Banthine cystometrograph, demonstrates normal bladder tonus and a bladder capacity of 450 cc with a strong voluntary voiding contraction. Sensation was normal and residual urine was absent. The cystometrograph following injection of Banthine shows no change in vesical tonus, capacity or sensation but the voiding contraction is abolished and the patient was unable to void any urine.

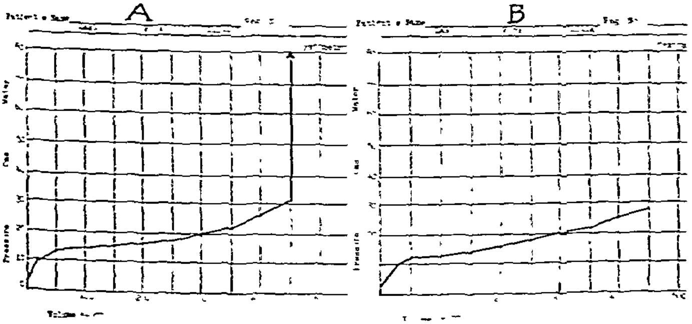

Fig. 1

B. *Uninhibited neurogenic bladder.* This type of bladder is observed in patients who have a lesion or defect of the pyramidal system. Symptomatically their complaints consist of frequency, precipitate micturition and incontinence. The patient can usually initiate urination voluntarily. Cystometric examination will reveal a bladder with normal tonus and sensation but with numerous uncontrolled voiding contractions. The functional capacity of these bladders is almost always reduced due to the uninhibited contractions occurring at low bladder volumes. Residual urine is absent. Ten patients with the uninhibited type of neurogenic bladder were selected for examination. The neurogenic bladders were associated with multiple sclerosis in 3 cases, with post-cerebrovascular accidents in 3 cases, with luetic paresis in 1 case, with post-cordotomy in 1 case, and with no known neurologic defect in 2 cases.

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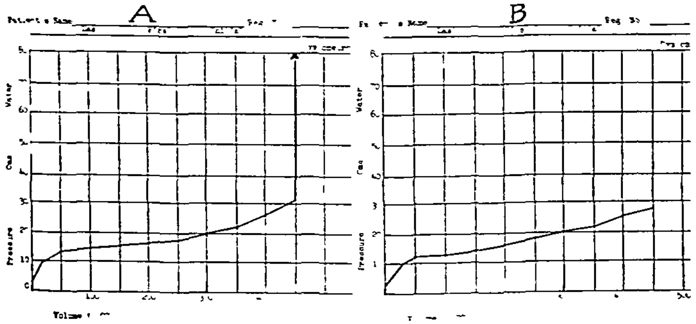

FIG. 1

B. *Uninhibited neurogenic bladder.* This type of bladder is observed in patients who have a lesion or defect of the pyramidal system. Symptomatically their complaints consist of frequency, precipitate micturition and incontinence. The patient can usually initiate urination voluntarily. Cystometric examination will reveal a bladder with normal tonus and sensation but with numerous uncontrolled voiding contractions. The functional capacity of these bladders is almost always reduced due to the uninhibited contractions occurring at low bladder volumes. Residual urine is absent. Ten patients with the uninhibited type of neurogenic bladder were selected for examination. The neurogenic bladders were associated with multiple sclerosis in 3 cases, with post-cerebrovascular accidents in 3 cases, with luetic paresis in 1 case, with post-cordotomy in 1 case, and with no known neurologic defect in 2 cases.

In figure 2, *A* can be observed the typical cystometric curve of an uninhibited neurogenic bladder in a patient with multiple sclerosis. Note the uninhibited bladder contractions! Bladder sensation and tonus are normal; bladder capacity is 100 cc. No residual urine is present. This patient complained of increased frequency of urination (every hour) and occasional incontinence. He was placed on oral Banthine, 100 mg. every 6 hours, for 4 days, at the end of which time he was re-examined. His frequency of urination had decreased to 4 times per day; *incontinence had vanished*. Figure 2, *B* demonstrates his cystometric determination after 4 days of Banthine therapy. Sensation and bladder tonus were unchanged, but the uninhibited contractions had disappeared, and the bladder capacity was now increased to 300 cc. The subject emptied his bladder with no residual urine. Banthine was then discontinued for 5 days and the patient again examined. Subjectively all of his symptoms had returned. The cystometrograph, (fig. 2, *C*) reveals that the functional bladder capacity had decreased to 75 cc volume and uninhibited contractions had returned.

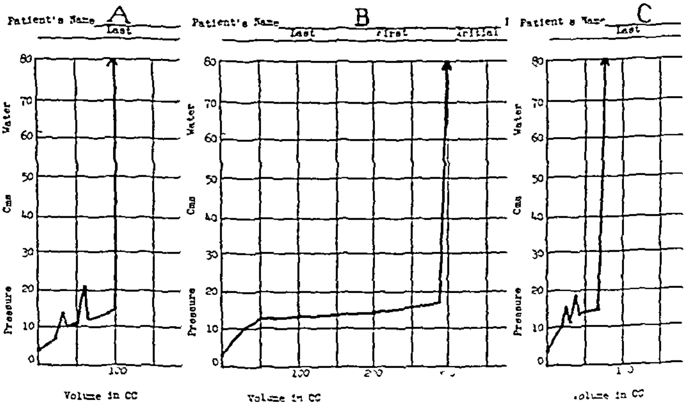

FIG. 2

Figure 3, *A* demonstrates the pre-Banthine cystometrograph of a patient with a left hemiparesis due to an old cerebrovascular accident. Bladder sensation and tonus are normal. Uninhibited contractions are present and bladder capacity is 150 cc. The patient complained of increased frequency of urination and incontinence. After 5 days of oral Banthine, 50 mg. every 6 hours, the patient's frequency of urination decreased and he became completely continent. Figure 3, *B* demonstrates his cystometric determination. Bladder capacity has increased to a volume of 265 cc and uninhibited contractions have disappeared. There was no residual urine.

All of the patients with uninhibited neurogenic bladders responded to Banthine in a manner similar to that of the two cases previously described, namely, a decrease in frequency of urination and disappearance of urinary incontinence. Two of the elderly patients developed partial urinary retention. Panendoscopic examination revealed obstructing prostatic hypertrophy in both subjects. Following transurethral prostatectomies the residual urines were decreased to within normal limits (under similar doses of Banthine).

C. *Reflex neurogenic bladder.* This type of bladder obtains in patients who have spinal cord lesions above the level of sacral spinal segments 2, 3, and 4 resulting in complete interruption of the ascending and descending tracts of the spinal cord. The reflex neurogenic bladder is devoid of sensation and exhibits uncontrolled voiding contractions. Urination cannot be initiated or inhibited in a normal voluntary manner. A fairly high residual urine is usually the rule in these patients.

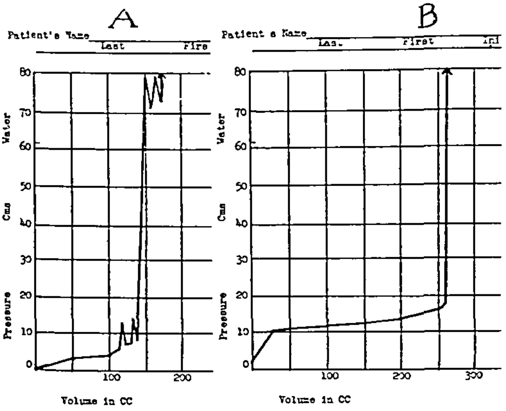

FIG. 3

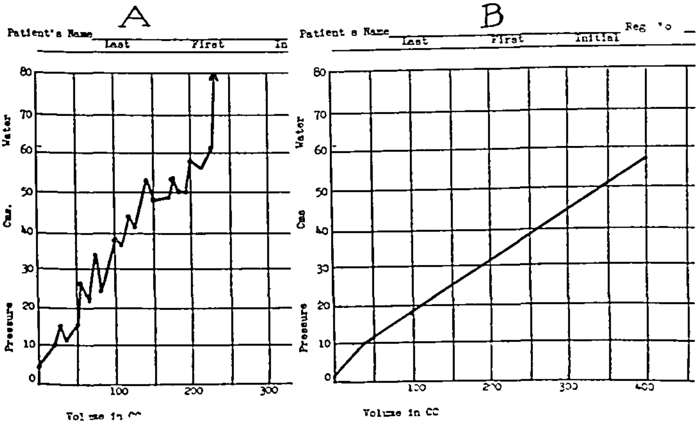

FIG. 4

Four patients with transverse myelitis and reflex neurogenic bladders were administered Banthine. All of the patients demonstrated an increase in residual urine with varying degrees of decrease in frequency of urination; apparent bladder capacity was increased. Figure 4, A reveals the cystometrograph of a female with a lesion at T4. All sensation is absent and numerous weak uninhibited bladder contractions are present. Figure 4, *B*, the cystometrograph obtained after 150 mg. of Banthine had been administered intravenously, reveals an increase in bladder capacity, a complete disappearance of the reflex contractions and complete urinary retention. The curve shows a linear relationship indicating that the actual bladder capacity is very small.

Observations on toxicity. No harmful side-effects were noted in any of the patients. Some of the patients on an oral dosage of 100 mg. of Banthine every 6 hours, observed that their mouths felt dry. Subjects who were given 150 mg. of Banthine intravenously complained of blurring of vision and dry mouths. It was interesting to note that dilatation of the pupils occurred immediately after injection of Banthine while the sensation of dryness of the oropharynx occurred several minutes afterward. There were no significant changes in pulse or blood pressure after intravenous Banthine administration.

DISCUSSION

It is apparent that the effect of Banthine upon any specific bladder, is dependent upon a) the dose of the drug, b) the drug sensitivity of a particular patient, and c) the status of the patient's bladder. The average normal bladder will usually not be affected by an oral dose of 100 mg. of Banthine every 4–6 hours or by an intravenous dose of 75 mg. If a patient has hypertrophied prostatic tissue partially obstructing the urethra so that the bladder is working at maximum capacity in order to empty itself, then any decrease in the number of motor impulses arriving at the vesical muscle (produced by Banthine) will result in varying degrees of urinary retention. Similarly, if the motor neurones of the nerves to the bladder are impaired by disease as in transverse myelitis, the bladder will not be able to empty itself effectively. Further impairment of the motor impulses by Banthine will result in increased urinary retention.

The uninhibited neurogenic bladder, uncomplicated by other factors, demonstrates a relative hyperactivity of the motor neurones. This situation is due to defective cerebral control because of a lesion in the pyramidal system which normally inhibits the motor neurones from responding to the afferent impinging proprioceptive impulses until the individual is ready to void voluntarily. The results obtained with moderate doses of Banthine in patients with uninhibited neurogenic bladders, indicate that the drug is capable of blocking the involuntary uninhibited contractions without affecting the final voluntary voiding contraction significantly. In symptomatic terms the patient's frequency, urgency, precipitate micturition and incontinence disappear without impairing the ability to empty his bladder completely. It should be noted that not all patients with an uninfected urine, frequency and enuresis have uninhibited neurogenic bladders; and, in these patients, Banthine will not be effective unless a dose large enough to produce some degree of urinary retention is given. The symptoms of this type of patient are usually on a psychogenic basis and therapy will lie in the realm of the psychiatrist. Their cystometric determinations will be found to be within normal limits.

Since Banthine does not affect bladder muscle tonicity but only voiding contractions, one must not hope to increase the capacities of bladders which are hypertonic due to cystitis or prolonged bladder drainage by the use of Banthine. However, if a bladder's capacity is small due to violent reflex contractions as in spastic paraplegics, then one can use large doses of Banthine in conjunction with distension of the bladder to increase rapidly the bladder capacity and eventually decrease the frequency of voiding contractions.

CONCLUSIONS

Banthine, in effective oral or intravenous doses, can block all the motor impulses to the bladder resulting in complete urinary retention.

In moderate doses Banthine is most effective therapeutically in the uninhibited neurogenic bladder, a condition frequently encountered in patients with *multiple sclerosis*, *hemiparesis* due to cerebrovascular accidents, luetic *paresis* (not tabes), *postoperative cordotomy* and congenital neurogenic *enuresis*. Banthine, in these patients, causes a disappearance of uninhibited contractions and results clinically in a decrease in frequency of urination with complete disappearance of urgency and incontinence without producing urinary retention.

Large doses of Banthine in conjunction with distention of the bladder is efficacious in increasing the bladder capacity of paraplegics with spastic reflex neurogenic bladders.

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VESICAL NECK OBSTRUCTION IN WOMEN

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Caulk in 1921 reported the first case in which a punch operation was done for relief of a contracture of the vesical neck in a woman. He removed several pieces of tissue from the vesical neck with his cautery punch, obtaining a very good result. He later reported 10 cases in which he had used his cautery punch in women, taking one to four pieces of tissue at a sitting. Other case reports and series then followed by Thompson, Nesbit, Fite, Winsbury-White and others.

Excluding neurogenic bladders, vesical neck obstruction in women may be defined as any condition which interferes with normal function and emptying of the bladder due to anatomical, pathological, or functional disturbance of the urethra and/or bladder base, and which produces varying degrees of urinary retention. The urethra is included since it is so intimately related to continence and the function of the bladder neck.

SYMPTOMS AND DIAGNOSIS

The diagnosis will often depend on the thoroughness with which women with urinary complaints are checked—especially those above 35 or 40 years of age. The symptoms associated with vesical neck obstruction vary a great deal. Complete or intermittent retention gives symptoms similar to those in men, causing no trouble in diagnosis. The larger group, having lesser symptoms and little, intermittent, or no residual urine, is harder to diagnose and probably often missed. Some with definite obstructive symptoms may be found to have no residual. Women who have had bladder trouble for years become so used to it that they may not at first give direct answers to questions concerning obstruction of the stream or its initiation. It is well to review the history thoroughly on several occasions. Some slowing of the stream and burning or discomfort at the end of urination, together with frequency and hesitancy, may represent just another attack of "cystitis" to the unhappy patient. Repeated residual checks are necessary during the remission of symptoms as well as at the peak of difficulty. Retention and residual may be associated with overdistention of the bladder during indulgence in alcoholic beverages. From the purely objective standpoint, vesical neck obstruction may be diagnosed when residual urine is consistently found in the absence of symptoms and diverticula.

The most common symptom is difficulty in voiding. Emmett lists the most common symptoms as:—frequency, dysuria, pain and burning on urination. Hematuria was given as the least common symptom.

Minor and transient degrees of vesical neck obstruction are usually seen by the general practitioner and gynecologist. These can usually be attributed to acute inflammation of the urethra, bladder, and peri-urethral tissues, and to

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Read at annual meeting, South Central Section, American Urological Association, Houston, Texas, October 31, 1951.

strictures and unusually small urethras. The management of these conditions presents no real problem. The ones not responding readily to treatment should be the object of investigation by the urologist.

When a case is to be studied, the study should be complete with pyelography and cystography, not just cystoscopy alone. Upper urinary tract dilation, though not common, is occasionally associated with vesical neck obstruction. Very occasionally diverticula of the bladder have been reported. Besides inspection of the bladder, the urethra and bladder neck should be carefully evaluated with the panendoscope or a direct vision cystoscope. The cystoscopic findings may be minimal or negative, and not in keeping with the patient's symptoms and residual urine. Trabeculation may be absent or minimal—just as found in careful routine cystoscopy on patients having complaints other than obstructive symptoms. The bladder neck may appear contracted yet give rise to no symptoms or residual.

The recommendations for transurethral surgery should rest largely on two factors: obstructive symptomatology and residual urine. Some surgeons will require consistent large residuals, while others will consider obstructive symptoms the prime factor. Other factors, as upper urinary dilation and infection, will often alter the picture in favor of surgery.

The obstructive symptoms usually come on during middle or later life. The ages ranged between 22 and 73 in the series reported by Thompson in 1939. In the series of 76 cases reported by Emmett et al. the highest incidence was in the fourth, fifth, and sixth decades. There were none in the second decade, and only six in the third.

ETIOLOGICAL FACTORS

A number of etiologic factors have been listed by the various authors: contracture of the vesical neck, hyperplasia of the vesical neck, stricture, carcinoma of the urethra or bladder, cystocele, etc. Many authors have listed chronic infection in the glands of the urethra and bladder neck as leading to fibrosis and obstruction.

John Neff reported 2 cases in which the cause of obstruction was "a loose, redundant ring of the mucosa surrounding the internal urethral orifice and which, under suitable conditions of observation, could be seen to jam the first part of the canal." Hugh H. Young concluded that "chronic inflammatory changes in the mucus membrane, in peri-urethral structures, and particularly in the glands, are often present and evidenced by swelling, by edema, by cystic and polypoid formations and sometimes by the development of definite bars or contractures of the vesical orifice." Braasch and Thompson suggested that "a nervous imbalance between the sphincters and the detrusor muscle leads to spasm of the sphincter and subsequently to hypertrophy, and, possibly hyperplasia of that muscle." Obstructions have developed following surgery and childbirth.

Folsom in 1931 called attention to the glands of the female urethra and bladder neck which were often the seat of inflammation and origin of symptoms. In 1943, Folsom and O'Brien presented an extensive study on the "Female Obstructing Prostate." They were of the opinion "that an infection harbored through the years in these glands is probably the cause of the bizarre pathologic picture seen in this portion of the female urethra."

In 1936, MacKenzie and Beck, after an extensive study on the female urethra and bladder neck, concluded that: "1) Chronic inflammation of the urethra and bladder neck is present in a higher percentage of adults than we have heretofore imagined. 2) Perimucosal structures about the bladder neck and posterior third of the urethra are acquired. 3) These acquired structures simulate prostatic tissue because they take their origin from the same type of embrylogic tissue, and thus have the same inherent properties."

An excellent study of the female urethra was made by J. W. Huffman. Necropsy material was taken from 11 subjects by excising the entire urethra and surrounding structures lying beneath the pubic arch, including the lower portion of the bladder and the anterior vaginal wall. Serial sections were made of each case and a wax model reconstruction of the entire urethra was made of three. Quoting from his conclusions, he says, "there seems every reason to believe that inflammation, irritation, and obstruction may result in the development of cystic enlargements of the intra-epithelial glands and small submucosal lacunae of the cysts which are sometimes found about the upper third of the female urethra."

Powell and Powell likewise found that in a high percentage of cases submucosal edema and hyperemia were associated with the inflammatory reaction which included submucosal inflammation, and lymphoid nodules.

MANAGEMENT

Conservative treatment by dilation, and other local therapy should be diligently carried out before a given case is listed for transurethral resection of the vesical neck. When resection is decided on, the vesical neck should be resected in its entire circumference, being careful not to carry the procedure too far distally or too deeply creating a vesicovaginal or urethrovaginal fistula. The procedure may be done with one of the high frequency loop resectoscopes, or one of the cold punch instruments, the author preferring the latter.

It is well known that multiple resections are sometimes necessary if immediate functional result is not satisfactory or if too large residual urine remains. Emmett has pointed out that although the initial result is good, the patient may again develop symptoms at a later date, and need further resection. From the series of 76 cases, Emmett reported 5 in which the residual had not been eliminated in spite of multiple resections of the vesical neck. One of these failures was attributed to scar tissue from pelvic surgery. In the other four cases no contributing cause could be found.

OTHER CONSIDERATIONS

There is another possible etiologic factor in vesical neck obstruction which the author would like to propose and discuss. It is believed that this factor readily explains why residual urines persist in some cases in spite of multiple and "adequate" resections in which the urethra is shortened and the vesical neck resected deeply. It can probably also explain why residual urine and obstruction may develop at a later date after an initial good result. It does not apply to cases in which the original anatomical contracted, infected, obstructing, or fibrosed vesical neck is resected once giving excellent results and permanent relief.

Before going into a discussion of this factor and some examples of it, there will be a brief digression by listing a few anatomical features and the important relationship of the bladder base to the pelvic floor in the physiology of micturition, which will help explain the mechanism of this factor.

The force exerted by the weight of the viscera plus the pressure exerted by the abdominal muscles is counteracted by the pelvic diaphragm which is composed of the levators ani and coccygeus muscles with their coverings of fascia. The bladder rests on the anterior vaginal wall and laterally on the levators ani, being anchored firmly only at its base and neck. The pubovesical ligaments insert into the neck of the bladder and the upper part of the urethra. Cunningham states: "The posterior wall of the urethra, except in its upper part, is very intimately connected with the anterior wall of the vagina, and as it approaches the external urethral orifice the urethra is practically embedded in the anterior vaginal wall."

From the extensive work on the levator ani muscle in man, W. C. Smith concluded that in both sexes the levator ani is composed of three distinct sets of fibers: pubococcygeus, iliococcygeus, and puborectalis, the latter forming the most massive part. He further noted that even in the nullipara there is a certain amount of variation of its fibers. The iliococcygeus is subject to much variation and is usually quite thin and aponeurotic in the aged. This condition is "responsible no doubt, for impaired functions of the pelvic diaphragm."

The importance of the integrity and function of the pelvic diaphragm is shown by the recent work of Muellner and Fleischner. They made an important contribution to our knowledge by the fluoroscopic study of the normal bladder during micturition, supplemented with spot films. The base of the resting bladder was found to be smooth and to lie just above the symphysis. The sequence of events in a normal person voiding is: 1) base of bladder descends sharply and becomes pointed; 2) after a short lag the detrusor contracts and micturition ensues, the base of the bladder rising slowly with emptying. Sequence of voluntary inhibition of the act leads to: 1) a sharp rise of the bladder base to a level slightly above the initial one; 2) the internal sphincter closes; 3) the base of the bladder becomes level and the detrusor relaxes. Study of micturition in patients who had the base of bladder fixed by cancer or by flaccid paralysis of pelvic diaphragm revealed a loss of the voluntary mechanism and substitution of an automatic one.

Further evidence of the importance of the pelvic diaphragm in the support of the urethra and base of the bladder in vesical function is shown by the recent reports of Marshall, Marchetti, and Krantz. Their simple vesico-urethral suspension, by the suprapubic approach, affords relief in a high per cent of stress [illegible] repairs from below have been unsuccessful. [illegible] cystographic study on 8 patients (who had this [illegible] women as controls that the restoration and fixation [illegible] and urethra in a normal position relieves stress incontinence [illegible] normal micturition. In continent women the base of [illegible] or just above the superior edge of the symphysis. [illegible] stress incontinence usually had the base of the bladder [illegible] upper border of the symphysis.

[illegible] anatomical structure and relationship in micturition [illegible] summarize these general facts: That in the normal relationship [illegible] the bladder base there is continence; that the loss [illegible] incontinence and that re-establishment of the normal [illegible] about continence once again. Since these facts have [illegible] the etiological factor which may have been overlooked [illegible] a retention instead of an incontinence may result [illegible] normal relationship, and proper restitution should give [illegible] The mechanism producing the "loss of normal relationship" [illegible] lies in the complicated pelvic floor where a relaxation in [illegible] a change in the normal structural and functional relationship [illegible] support of the bladder base and urethra, or the proper relationship [illegible] the urethra and bladder neck and base.

[illegible] may be produced by trauma, childbirth, pregnancy, surgery, [illegible] of atrophy in muscle or fascia. Just as certain muscles or [illegible] in the aged will atrophy or become weaker, so may [illegible] complicated levator ani and or its fascia undergo differential [illegible] while the remainder holds. These causes or a combination [illegible] lead to a kinking or obstruction of the urethra as illustrated in [illegible] The resulting lack of normal support, instead of some form [illegible] the opposite—urinary retention and obstruction.

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Dr. C. M. Crigler in a personal communication told me of a similar case. A woman of about 60 years of age developed urinary obstruction. Two vesical neck resections did not relieve the obstruction and residual urine, but a subsequent repair of a moderate cysto-urethrocele gave her complete relief.

Dr. T. P. Shearer told me of a case which falls in this category. A 38-year-old multipara developed complete retention. She found that she could void when prone or lying on her side. Examination revealed only a moderate cysto-urethrocele and what seemed to be some buckling of the urethra. Conservative treatment by sounds did not afford relief. however. An anterior repair of the cysto-urethrocele gave complete relief. The author feels that primary surgery on the vesical neck would not have relieved her.

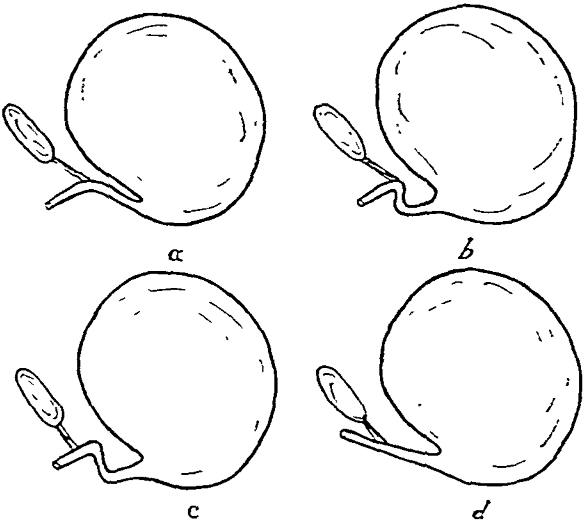

FIG. 1

Occasionally very large cystoceles will lead to a disturbed bladder function and residual urine. The altered bladder function is probably due primarily to a change in the urethrovesical angle.

It is possible that the amount of relaxation in the bladder neck region necessary to produce obstruction may not be obvious on gross examination. just as a slight relaxation in a nullipara may result in stress incontinence. If the displacement is just at the vesical neck. one would expect resection at this point to give good results—as transurethral resection happens to in the majority of cases. Then at a subsequent date. if there is added relaxation at this point. there will be renewed obstruction and symptoms recurring—in this type removal of a little more tissue will again give a good result. But if the point of tension is in the mid or distal urethra. then several resections can be carried out without incontinence, even when repeated repairs from below have been unsuccessful. Marchetti showed by means of cystographic study on 8 patients (who had this procedure) and on 5 continent women as controls that the restoration and fixation of the vesical neck and urethra in a normal position relieves stress incontinence and establishes normal micturition. In continent women the base of the bladder was found at or just above the superior edge of the symphysis, whereas those having stress incontinence usually had the base of the bladder located well below the upper border of the symphysis.

In view of the foregoing anatomical structure and relationship in micturition and continence, we can summarize these general facts: That in the normal relationship of the pelvic floor to the bladder base there is continence; that the loss of this relationship leads to incontinence and that re-establishment of the normal relationship brings about continence once again. Since these facts have been shown to be true, the etiological factor which may have been overlooked heretofore is that similarly a retention instead of an incontinence may result from the loss of the normal relationship, and proper restitution should give *normal function. The mechanism producing the "loss of normal relationship"* and hence obstruction lies in the complicated pelvic floor where a relaxation in some part of it produces a change in the normal structural and functional relationships of the support of the bladder base and urethra, or the proper relationship between the urethra and bladder neck and base.

These changes may be produced by trauma, childbirth, pregnancy, surgery, and senile changes of atrophy in muscle or fascia. Just as certain muscles or muscle groups in the aged will atrophy or become weaker, so may a part of the complicated levator ani and/or its fascia undergo differential atrophy and failure while the remainder holds. These causes or a combination of them will lead to a kinking or obstruction of the urethra as illustrated in figure 1, *a*, *b*, and *c*. The resulting lack of normal support, instead of some form of incontinence, is just the opposite—urinary retention and obstruction.

It is not uncommon to see women who have little or no urinary difficulty in spite of cysto-urethroceles. Though the axis of the urethra is changed, it is still probably unchanged with respect to the bladder base and neck, permitting normal function (fig. 1, *d*). But let us suppose that the base of the bladder, vesical neck, and proximal urethra descend in the cystocele, the distal part of the urethra remaining in its normal position thereby producing an angulation halfway down the urethra—fig. 1, *b* or *c*. If this vesical neck and proximal third of the urethra were resected, the patient would still have an obstruction located just below the new vesical neck.

In support of this proposed etiology the following case which the author saw several years ago is presented: An elderly multipara became suddenly obstructed. Urethral dilatation and catheter drainage gave no relief. No neurogenic factor was present; upper urinary tract was normal; bladder and bladder neck were not particularly remarkable; a cystocele grade 1 or 2 was present (basis 1 minimum and 4 maximum). Two vesical neck resections opened the vesical neck widely but still did not permit the patient to void. Without the catheter the retention would become marked, but no overflow incontinence would ensue to relieve the patient. In further examination of this patient it was found that one or two fingers giving vaginal support in an upward and backward direction would allow the urine to gush out.

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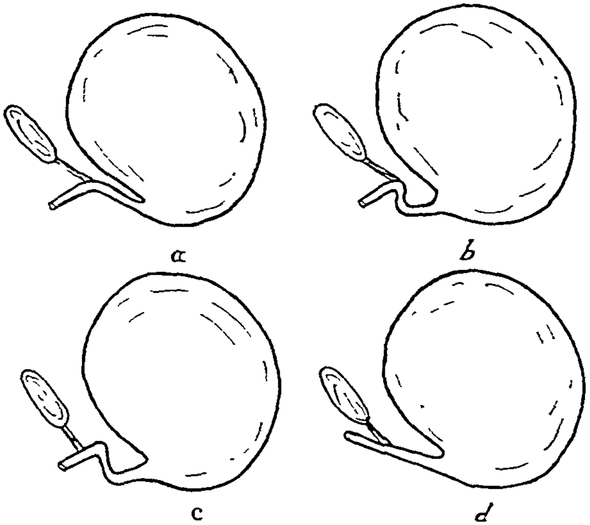

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Therefore the author suggests that when one or two resections of the vesical neck fail to yield good results and elimination of residual urine, an underlying cause should be sought in the status of the pelvis floor supporting the base of the bladder and urethra. *If a defect is found, it would probably be best to* attempt correction of this rather than to pursue further vesical neck resection and risk incontinence. Careful case study and cysto-urethrograms may give us the clue for differentiation and aid us in proper selection of the initial operation. Some patients now receiving vesical neck resections might be as easily relieved of their symptoms by a Kelly or Marchetti type of operation, as was Dr. Shearer's patient.

SUMMARY AND CONCLUSIONS

Vesical neck obstruction in women varies between minimal degrees and complete retention. Cystoscopic findings do not always correlate well with the symptoms and residual urine. When conservative treatment fails, vesical neck resection should be performed. The indications for resection should be either one or a combination of the following: 1) visible obstructive tissue at the vesical neck, 2) definite obstructive symptoms, 3) consistent significant residual urine of several ounces, 4) residual urine which is infected.

If the symptoms and residual urine are not altered much, a second resection may be cautiously tried. Then, if the symptoms are not entirely relieved, evidence of some other etiologic factor should be sought. In some cases it may be well first to give the bladder and urethra adequate support before embarking on transurethral surgery. As the urologic diagnostic acumen improves, this surgery will come to lie in the field of the urologist.

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BLADDER NECK OBSTRUCTION IN THE YOUNG MALE ADULT

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Congenital obstruction at the vesical neck in infants and children and those of an acquired nature in the aged are generally well recognized clinical entities, and the literature is replete with references to etiology, pathology and therapy of these conditions. The purpose of this paper is to emphasize the existence of obstructive pathology in the intermediate age group, and to stress the need for more accurate diagnosis and more adequate therapy.

In the last 2 years 26 young men suffering from median bar and bladder neck contracture have been admitted to the Urology Section. Ages ranged from eighteen to thirty-four with the average being twenty-four. These entities probably are seen more frequently in the armed forces because of the large concentration of young men, and because of the tendency for personnel to present themselves for investigation of all physical complaints.

The symptomatology is not constant and is not pathognomonic of bladder neck contracture or of median bar. Predominant complaints are those associated with bladder neck disease from any cause. Nocturia, diurnal frequency, dysuria and urgency are the most common. A history of hematuria is obtained with surprising frequency and is almost always either initial or terminal. Total hematuria as encountered in one case is usually associated with other disease. Low back pain and lower abdominal pain occur about thirty per cent of the time. Premature ejaculation occurs in approximately twenty per cent of this series, but there is no other indication of sexual abnormalities. Fever, urethral discharge, enuresis, rectal pain and changes in the urinary stream are encountered with less frequency. Acute urinary retention requiring catheterization has occurred twice (table 1).

The duration and severity of symptoms frequently bear little correlation with demonstrable disease. The duration of symptoms varies from childhood to within one year of hospitalization. The onset in about seventy-five per cent is dated within five years.

Many of the patients have been treated previously for a variety of conditions. "Kidney disease" has been a common diagnosis. The remainder have been treated for prostatitis, urethral stricture, chronic cystitis, chronic pyelonephritis and glomerulonephritis. Very few of them have received a urological survey complete with endoscopy. Chronic cystitis has been the common finding in those who have undergone cystoscopy. Only about twenty per cent will admit having had gonorrhea and having received treatment for it (table 2).

The physical findings are inconclusive when unaccompanied by laboratory, x-ray and cystoscopy. Rectal examination usually elicits a prostate gland which is normal or smaller than normal in size. In a few cases there may be a definite impression of some thickening of the gland but not enough to be called a hyper-

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Read at annual meeting, South Central Section, American Urological Association, Houston, Texas, October 31, 1951.

trophy. Prostatic secretions in 50 per cent of cases are infected, that is, more than five white blood cells can be visualized per high power field. Urine in 50 per cent of cases is grossly, microscopically and culturally negative. The others exhibit shreds and white blood cells in the first glass. Organisms cultured from the infected urine are predominantly of the gram negative colon group. Microscopic hematuria is found in three-fourths of those who offer this as a complaint.

TABLE 1. *Symptoms, 26 patients*

	NO.	PER CENT
Nocturia	24	92.0
Diurnal frequency	15	57.7
Hematuria	11	42.3
Dysuria	10	38.5
Urgency	8	30.8
Hesitancy	8	30.8
Lower abd. pain	8	30.8
Low back pain	7	27.0
Premature ejaculation	5	19.2
Urethral discharge	4	15.4
Fever and chills	4	15.4
Enuresis	3	11.5
Spraying	3	11.5
Rectal pain	2	7.7
Acute retention	2	7.7

TABLE 2. *Conditions for which previously treated, 26 patients*

	NO.	PER CENT
Kidney disease	9	34.6
Chronic prostatitis	8	30.8
Urethral stricture	4	15.4
Chronic pyelonephritis	3	11.5
Chronic glomerulonephritis	1	3.8

TABLE 3. *Urinary findings, 26 patients*

	NO.	PER CENT
Normal	13	50.0
Infected	13	50.0
Hematuria	7	27.0
Digital examination of prostate		
Enlarged	9	34.6
Normal or smaller than normal	17	65.4
Prostatic secretions		
Normal	13	50.0
Infected	13	50.0

Significant residual urine has not been a factor in this series, but two patients have had a consistent residual of as much as 50 cc (table 3).

Urograms have been helpful in confirming the clinical impression of bladder neck obstruction, but have been of little value in determining the exact type. Urograms have demonstrated trabeculation, diverticula, dilatation of the lower ureters and hypertrophy of the interureteric ridge resulting from obstruction. Urethrograms have not been diagnostic, but in some cases are suggestive of the type of obstruction (fig. 1).

Accurate diagnosis is made only through careful and thorough use of the cystoscope and panendoscope. Some difficulty may be encountered in introducing an instrument through the bladder neck. After rather forceful depression of the hilt of the instrument, it can frequently be felt riding over an obstruction. Inspection will reveal a bar or dam across the inferior portion of the vesicourethral orifice with depression of the trigone proximally and of the prostatic urethra distal to it. The circumference of this orifice not occupied by the bar is usually contracted so that the outlet may consist only of a "pin-point" opening. In this series the bar and contracture are almost always co-existent, and one rarely exists without the other. In addition to the bladder neck, the bladder itself must be well visualized because of the not unusual contribution of a distorted trigone to the obstruction. Marked hypertrophy of the interureteric ridge, which may be undermined and floating, is greatly obstructive. Shortening of the trigone may place this hypertrophied ridge in juxtaposition to the median bar so that the two represent virtually a continuous structure. Additional evi-

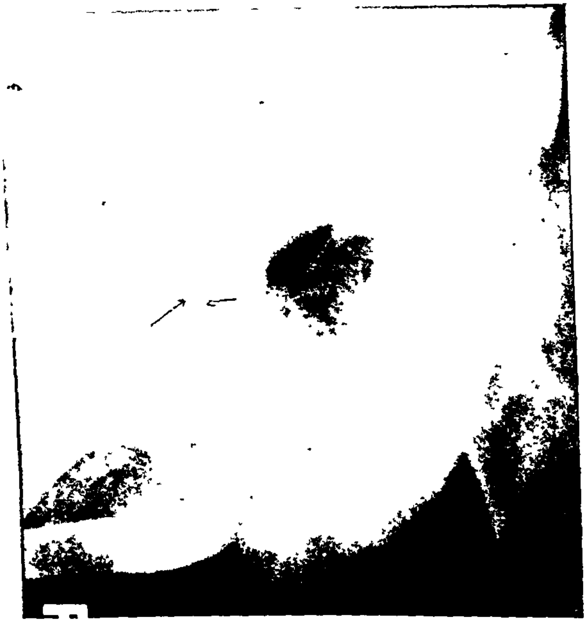

FIG. 1. Urethrogram showing forward displacement of prostatic urethra due to median bar and mild defect due to contracture.

dence of a bar may be obtained by rectal palpation of the prostate over an indwelling instrument. Often a transverse thickening measuring an estimated one to two centimeters in thickness can be detected at the base of the gland (fig. 2).

Other existing abnormalities detected on cystoscopy or urethral calibration have been bladder trabeculation and diverticula, chronic cystitis, chronic posterior urethritis with involvement of the verumontanum, shortening of the prostatic urethra and urethral stricture. Chronic infections of the bladder and urethra are often manifest by granulation tissue which bleeds easily when touched. In 1 case there were numerous large inflammatory polyps. These infections were the probable sources of hematuria (table 4).

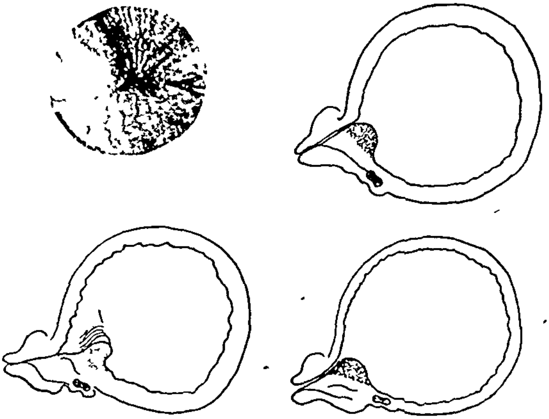

FIG. 2. Cystoscopic appearance of contracted bladder neck. Drawings depict median bar, hypertrophied interureteric ridge and a composite of the two.

TABLE 4. *Associated conditions, 26 patients*

	NO.	PER CENT
Bladder trabeculation	12	45.4
Urethral stricture	7	27.0
Chronic cystitis	6	22.7
Chronic posterior urethritis	5	19.2
Diverticulum	2	7.7
Ureteral dilatation	2	7.7

Treatment is both medical and surgical. Medical treatment is directed toward the eradication of all infections. Urinary infections have responded to antibiotics administered after sensitivity tests. Chloromycetin, aureomycin and the sulfa preparations have proved very effective. The sulfa drugs, massage and hot sitz baths are effective in clearing prostatic infections. In the more persistent chronic involvements of the prostatic urethra and bladder, those with granulations or hypertrophic inflammatory tissue, more vigorous therapy is required. Urethral dilatations and instillations of 1 per cent silver nitrate are excellent in clearing posterior urethral infections. Dilatation of the stenosed vesical neck with sounds or Kollmann dilators accompanied by frequent irrigations and instillations of 10 per cent argyrol or 1:5000 potassium permanganate are moderately effective in cleaning up the bladder. In order to be at all effective the medical treatment must be accompanied by correction of urethral stenoses by meatotomy and by progressive dilatation of strictures.

Eight of the cases have responded at least temporarily to medical treatment and have been returned to duty. The basic disease at the bladder neck, however, has not been relieved, and recurrence and progression of symptoms must be anticipated. The remainder experienced little or no relief of symptoms and surgical intervention was necessary.

Transurethral resection has been the surgical procedure of choice. Suprapubic removal, while not used in this series, has proved unsatisfactory in other similar cases. The retropubic technique has not been used because it is believed inadequate in circumferential lesions of this type. In the vast majority of cases obstruction is not limited to one segment and surgery must be performed throughout the entire circumference of the orifice. The obstructing tissue is not well delineated as in benign hypertrophy and enucleation is most difficult; also the surgical effort is directed toward the bladder neck and trigone with as little disturbance of the prostatic urethra as possible.

TABLE 5 *Pathology, 26 patients*

	NO.	PER CENT
Benign hyperplasia of prostate	11	42.3
Chronic fibrous prostatitis	6	22.7
Chronic cystitis	3	11.5
Chronic urethritis	2	7.7
Prostate	1	3.8
Acute focal prostatitis	1	3.8
Polyps, inflammatory type	1	3.8

Resection of the bar or of the contracture exclusive of the other constitutes inadequate therapy. Often one loop of tissue removed from the center of the bar will result in marked expansion of the orifice. This phenomenon should not preclude the remainder of the operation. In the event of confluence of the bar and the interureteric ridge, the center of the ridge may be resected at the same time. A distinct but hypertrophied ridge must be resected in the center to further relieve obstruction. The orifices which may have been drawn toward the midline and toward the vesico-urethral orifice often retract to a more normal position. At the completion of surgery the vesico-urethral orifice should be wide open, roughly circular, and the floor of the bladder and prostatic urethra should be virtually on the same plane with no intervening tissue.

The amount of tissue removed varies from 2 to 5 gm. The severity of symptoms then would appear to be more dependent on the nature and location of the obstructing tissue rather than on the quantity. The pathological diagnoses show a predominance of benign hyperplasia and inflammation. The frequency with which the diagnosis of benign hyperplasia is made is surprising (table 5).

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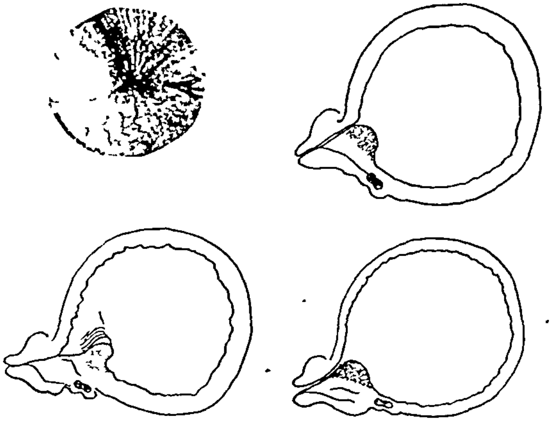

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The most serious postoperative complication has been hemorrhage. Four of the eighteen operated cases bled rather profusely in the immediate postoperative period. This is a higher percentage than is ordinarily encountered in resection of large glands and may be explained by a tendency to consider this a small procedure not worthy of the meticulous care afforded larger glands. Such a tendency is a grave error. One secondary hemorrhage occurred on the thirteenth day, and one urethral stricture directly attributable to surgery has responded to periodic dilatations. Two infections due to Aerobacter aerogenes and Pseudomonas have responded to chloromycetin and mandelic acid. No disturbances of libido or of sexual capacity have resulted.

The postoperative follow-up care of these patients is just as important as it is in those who have had large glands removed. The basic disease is often due to contracture of fibrous tissue. Even though the obstructing element has been removed, bladder neck dilatations should be performed at monthly intervals for 6 months. Any infection must be carefully controlled. With one exception all personnel have experienced relief of symptoms and have been returned to duty. This one man had a severe congenital stricture of the penile urethra which had led to persistent urinary symptoms, pyuria, hematuria, and necessitated his separation from the service. Enuresis has at least temporarily been relieved. Pain in the low back, lower abdomen and rectum has subsided in all but 2 cases and these have experienced marked relief. These two had inflammatory involvement of the seminal vesicles which may have prevented complete relief.

CASE REPORTS

Case 1. A 21 year old white man presented himself for investigation of urinary complaints of 2 years' duration. Symptoms included nocturia 2 to 3 times, lower abdominal distress, diminished force of the stream, mild hesitancy and three episodes of urinary tract infection which had responded to medical treatment under the diagnosis of "kidney disease." A thorough urological examination had never been performed. The urine and prostatic secretions were normal. Excretory urograms exhibited bilateral dilatation of the ureters suggestive of lower tract obstruction (fig. 3). Cystoscopy and panendoscopy revealed severe contracture of the vesico-urethral orifice with moderate median bar. Transurethral resection resulted in complete relief of symptoms and the patient was returned to duty.

Case 2. A 24 year old soldier was returned from an overseas station with a diagnosis of "bladder trouble." On repeated questioning he steadfastly denied all urinary symptoms except for one episode of frequency and dysuria. At that time a urinary tract infection responded to sulfathiazole. A cystoscopy revealed "bad bladder trouble," and he was returned to the Zone of Interior. The urine was not infected, but there was a constant residual of about fifty cubic centimeters. Excretory urograms outlined a normal upper urinary tract but indicated a trabeculated bladder with a diverticulum measuring 4 cm. in its greatest dimension. This was proved by cystogram and cystoscopy. Panendoscopy exhibited a contracture and median bar of such severity that the vesico-urethral

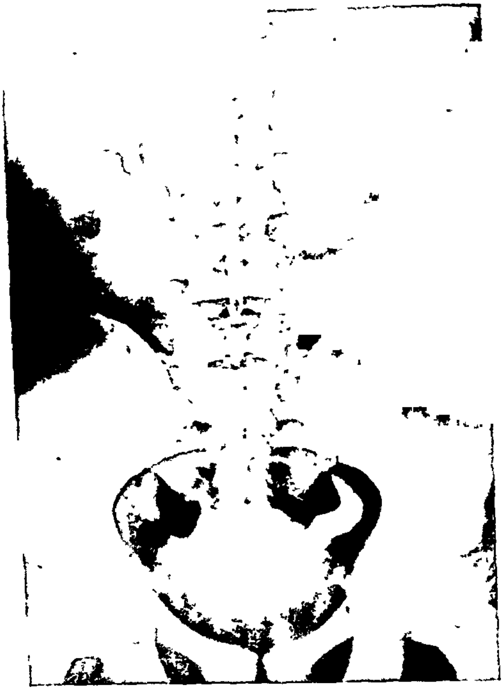

FIG. 3. Excretory urogram showing dilatation of both lower ureters and hypertrophy of interureteric ridge secondary to bladder neck obstruction.

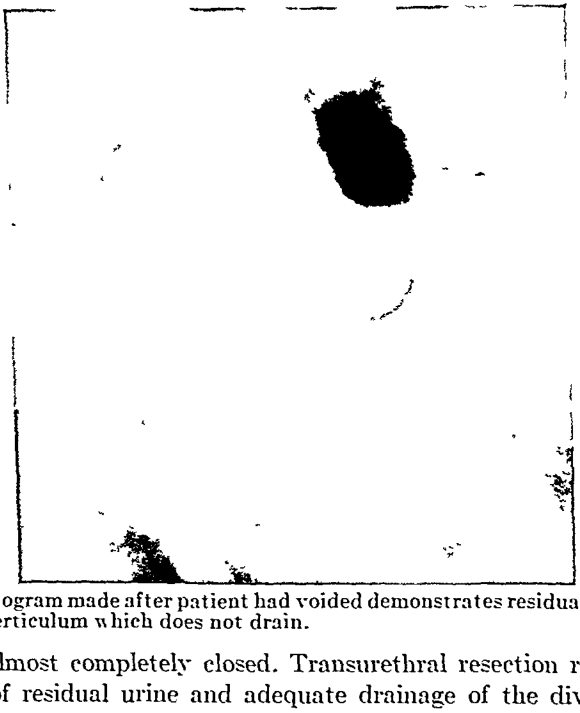

FIG. 4. Cystogram made after patient had voided demonstrates residual urine, trabeculation and a diverticulum which does not drain.

orifice was almost completely closed. Transurethral resection resulted in complete relief of residual urine and adequate drainage of the diverticulum. The diverticulum has not increased in size, caused symptoms, or contributed to recurrence of infection and has not been removed (fig. 4)

Case 3. A 24 year old Negro soldier was admitted with the complaints of "hard to pass water" and "bloody urine." For about eighteen months he had had nocturia 2 to 3 times with increasing difficulty in starting urination. Intermittently for 6 months he had passed bloody urine containing occasional clots. This had been attributed to infection, and he had received numerous "shots and pills" without relief. After admission the urine consistently contained white blood cells, red blood cells and the cultures grew Aerobacter aerogenes. Excretory urograms visualized normal kidneys and ureters, but the bladder shadow was mottled and irregular near the neck. Panendoscopy exhibited a severe contracture and small median bar with severe chronic cystitis manifested by papillary hypertrophy of chronic inflammatory tissue. The infection and hematuria remained present after administration of chloromycetin and aureomycin and cultures remained positive. Transurethral resection effectively relieved the obstruction. Many of the inflammatory polyps were resected and fulgurated. Adequate hemostasis was difficult to achieve, and because of bleeding the operation was discontinued prior to completion. Three weeks later a resectoscope was again used to remove all polyps. Subsequently infection and hematuria have subsided and cultures are negative (fig. 5).

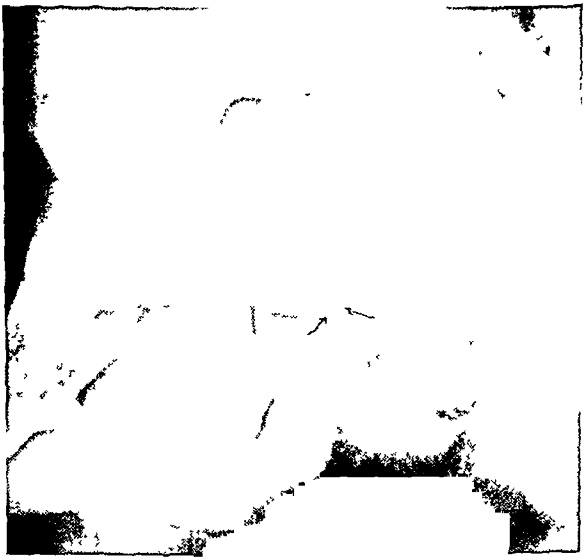

FIG. 5 Urethrogram demonstrating defect at bladder neck due to contracture. Irregularity of bladder shadow is due to large inflammatory polyps.

COMMENT

Median bar and bladder neck contracture in the younger age group are probably more common than is generally recognized. The exact etiology is obscure, but chronic infection is probably a factor. Chronic glomerulonephritis, pyelonephritis, "kidney disease" and prostatitis are infectious conditions for which these individuals have previously been treated. The pathological diagnoses of chronic fibrous prostatitis, chronic cystitis, chronic urethritis, acute focal prostatitis, chronic cystitis, chronic urethritis, acute focal prostatitis, and inflammatory polyps further suggest the influence of infections. Since only approximately twenty per cent admitted venereal disease, its role is inconclusive, but this may have been the original cause of some of the prostatic and urethral infections.

This series of cases is too small to draw any definite conclusions, but the pathological diagnosis of benign prostatic hyperplasia appears too often to be overlooked as a primary etiological factor. Many more cases will have to be studied before this condition can be classed as a frequent offender in bladder neck obstruction in young individuals.

SUMMARY

A summarization of twenty-six cases of median bar and bladder neck contracture in young men from eighteen to thirty-four years of age has been presented. These conditions are often missed entirely and improper treatment is frequently employed under a wrong diagnosis. The symptoms are not pathognomonic, and the diagnosis can be made only by thorough urological investigation. Surgery in most instances gives gratifying results. Based on the history, physical findings and pathological diagnosis, infections and benign prostatic hyperplasia have been offered as possible etiological factors.

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VESICAL NECK OBSTRUCTION WITH OVER 8000 CC RESIDUAL URINE

REXFORD G. CARTER

Excessively large amounts of residual urine must be very rare or very common. A search of the literature as far back as 1911 shows only a few cases reported, and none over 5000 cc.

Some reports stated that the bladder contained massive residual, but did not give the quantity found.

Orr, in 1937, reviewed the literature and made the distinction between atony due to neurogenic causes and that due to bladder neck obstruction. In the first, the bladder wall is smooth, symmetrical and not trabeculated. In the latter type, trabeculation is produced by hypertrophy of the muscle bundles resulting in an uneven bladder outline. Cellules and diverticula also develop frequently.

In bladders of this type with very large residuals, removal of the obstruction has not been sufficient to restore good function with normal capacity and no residual. More recent papers by Crabtree and Muellner, and by Fish confirm the earlier reports. All agree that best results are obtained by removal of two thirds or more of the bladder wall which leaves a bladder of normal capacity and capable of emptying.

CASE REPORT

S. H. B., aged 67, was first seen January 19, 1951, with a tremendously distended abdomen. He had been dribbling a few drops of urine almost constantly for 2 days. During the previous 4 months he had a slow stream with frequency, and nocturia of 4 to 7 times. The past history was of no importance.

The patient was having only mild discomfort from distention. The entire abdomen was hard and tight from the ziphoid to the symphysis. The prostate was of normal size but firm. There was no fixation or other evidence of malignancy. A catheter was passed into the bladder easily and during the next hour over 8000 cc of urine were obtained. During this time he showed no evidence of discomfort or shock. Warm water (2500 cc) was placed in the bladder and the catheter clamped. He was sent to the hospital and instructions given to release 400 cc of fluid from the bladder every 30 minutes. Four hours later he complained of a full bladder although over 3000 cc had been removed. The catheter was unclamped and 4000 cc of urine released. No further attempt at decompression was made, and large quantities of urine drained from the catheter during the next 48 hours. There was no discomfort, chills, fever or shock, and no blood appeared in the urine.

Laboratory data: Red blood cells, 4,260,000; hemoglobin, 12 grams, or 77 per cent; white blood cells, 10,200 with 71 per cent total polymorphonuclears. Nonprotein nitrogen, 40. Urine: Specific gravity 1.016; sugar, negative; albumin 1

Read at annual meeting, South Central Section, American Urological Association, Houston, Texas, October 31, 1951 plus. Microscopic examination: Many pus cells and red blood cells present. Culture produced E. coli., and a nonhemolytic streptococcus.

The patient was kept on constant drainage for 2 days and prepared for operation.

Cystoscopy under anesthesia showed a median bar enlargement of the prostate. Several small stones 0.5 to 1 cm. in diameter were seen in the bladder. Another oval stone about 1 by 1.5 cm. was lying between the bladder neck and verumontanum. This stone appeared to block the urethra more completely than the median bar. These stones were removed without difficulty. The bladder neck was then resected in its entire circumference with a total of 11 grams of tissue removed. The pathologist's report showed prostatic hypertrophy and chronic urethritis.

The catheter was removed on the afternoon of the sixth day. He voided several times during the night, and the next morning had 2000 cc of residual. The catheter was replaced. Two weeks after operation the bladder capacity was 2000 cc. He voided 800 cc spontaneously, leaving 1200 cc residual. The catheter was left in. At the end of the third week, the capacity was 1000 cc and the residual 500 cc. Again the catheter was left in. At the end of the fourth week the residual was 325 cc, and the catheter was removed. At the end of the 5 weeks he was voiding well and had no residual whatever (fig. 1).

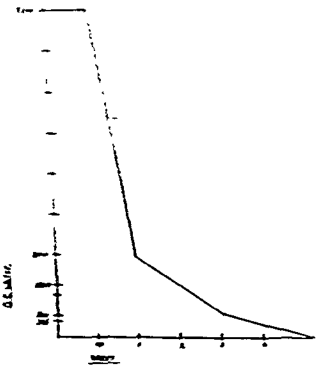

FIG. 1

FIG. 2

This man was last seen on August 28, 1951. At that time he was voiding easily and getting up once or twice at night. The urine was very cloudy. The bladder capacity was 450 cc with the first desire to void at 350 cc. The maximum voluntary pressure on a full bladder was 35 mm. of mercury. There was no residual urine.

An excretory urogram showed good function in 5 minutes and no abnormalities of the upper tract. No stone shadows were seen.

Cystoscopy showed the bladder wall with many folds and crevices but no diverticula. The ureteral orifices were normal and urine spurted out normally. There was no apparent obstruction at the bladder neck. A cystogram was made using 300 cc of sodium iodide. This film showed extreme irregularity of the bladder resembling extravasation. There was no reflux up the ureters (fig. 2).

DISCUSSION

This case does not fall into the pattern described by Orr, Fish, Crabtree and Muellner. The capacity is not increased and there is no residual; indicating a good functional result. However, the urine remains grossly infected, and the cystogram shows marked deformity of the bladder. For these reasons a partial bladder resection seems indicated.

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LEUKOPLAKIA OF THE URINARY BLADDER AND ITS ASSOCIATION WITH CARCINOMA

DAVID B. CONNERY

Leukoplakia of the urinary bladder has always been considered a relatively rare disease. It was diagnosed approximately 150 times in 1,500,000 admissions to the Mayo Clinic between January 1, 1915, and January 1, 1947, an incidence of 1 in 10,000 admissions. From my experiences in this study, I believe it to be decidedly more common than previous figures have indicated. I have also learned to respect it as a disease with extremely severe consequences as to morbidity and mortality.

Leukoplakia of the urinary bladder was first described by Rokitansky[1] in 1861. It has been a subject of controversy ever since. There is no officially accepted criteria for its diagnosis. The criteria of one author are entirely different from the next.

The question as to whether leukoplakia is a precancerous lesion is equally controversial, as witnessed by differences in opinions as expressed by Thompson and Stein,[1] who have stated that in their opinion in not more than 6 per cent of the cases does malignancy develop. Montgomery,[2] of the same clinic, states unequivocally that in not less than 20 per cent does an epithelioma eventually develop. Most writers in general agree with Montgomery's figure.

Because of this wide difference in opinions, especially as to its status as a precancerous lesion, it was believed that a study of leukoplakia of the urinary bladder, as seen at the Mayo Clinic, would be of value. Accordingly, all cases diagnosed as leukoplakia of the urinary bladder from January 1, 1915, until January 1, 1947, were abstracted and studied (tables 1, 2, 3.)

My first problem was to accept definite criteria for its diagnosis. Here, I met the widest differences in opinions, varying from that of mere squamatization as given by Robson[3] and accepted by Putschar[4] and Marion[5] to the very exacting criteria demanded by Montgomery,[2] which include hyperkeratosis, increase in the stratum granulosum, acanthosis, lymphatic infiltration in the upper cutis, liquifaction necrosis of the basal layer, and destruction of the elastic fibers of the corneum.

From my own observations of these tissue sections, I came to agree with the opinions of Gelhorn,[6] Kutzmann,[7] and McDonald.[8] McDonald states his criteria very simply as cornification of a noncornifying membrane.

It can best be characterized as hypertrophy of all the layers, with keratiniza-

[1] Rokitansky, quoted by Thompson, G. J. and Stein, J. J.: Leukoplakia of the bladder and a report of 34 cases. J. Urol., 44: 639–649, 1944.

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Read at annual meeting, South Central Section, American Urological Association, Houston, Texas, October 29, 1951.

tion, squamatization, and cornification until that mucosa can scarcely be differentiated from true epidermis. It is true metaplasia, as expressed in the words of Haythorn,[9] "the transformation of one well differentiated tissue into another of equally well characterized type, but different morphologically and functionally."

In passing, it is of interest to recall that leukoplakia, which is a disease typical of ectoderm, in the urinary bladder arises from tissue which embryologically arises from mesoderm and entoderm.

Leukoplakia has been described on the mucosa of the tongue, gums, sinuses, tympanic membrane, nose, esophagus, gallbladder, rectum, vagina, uterus, and the entire urinary tract.

TABLE 1. *Grading of six carcinomas of the urinary bladder associated with leukoplakia*

GRADES	I	II	III	IV
Males	0	2	3	0
Females	1	0	0	0

TABLE 2. *Age incidence of carcinoma of the bladder in association with leukoplakia*

	MALES	FEMALES
50-60	3	1
60-70	3	

TABLE 3. *Age incidence of leukoplakia in males and females*

	MALES	FEMALES
20-30	2	1
30-40	2	1
40-50	6	4
50-60	12	4
60-70	8	3
70-80	2	0
	32	13

In the past it has been described under the following terms: leukoplakia, metaplasia, proplasia, epithelial metaplasia, pachydermia, xerosis, membranae mucosae, leukokeratosis, tylosis, epidermal plaques, and the erythroplasia of Queyrat.

The following plan of study was then adopted:

1) The diagnosis of leukoplakia of the urinary bladder was listed a total of 151 times in the combined files of Surgical Pathology and Pathological Anatomy. It was found that in two incidences the cases were coincidental, so there were actually 149 cases available. These were carefully abstracted and studied.

2) The second project was the examination of tissue sections from 400 blocks of tissue made for Dr. Herbert Henkel from 100 urinary bladders. From these bladders he had taken four sections: one from each lateral wall, one from the posterior wall, and one from the trigone. These bladders were considered grossly normal. They were studied for the incidence of leukoplakia in normal bladders.

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[9] Haythorn: On metaplasia of bronchial epithelium. J. Med. Research, **26**: 523, 1912

3) The third part of this program proved of little value. One hundred and seventy-two sections of bladder tumors from a recent publication of Drs. McDonald and Thompson were obtained and studied with a view of finding the incidence of carcinoma associated with these tumor cases. The reason for its failure was due to the fact that almost all sections were made of tumor tissue only and no adjacent tissue available to study.

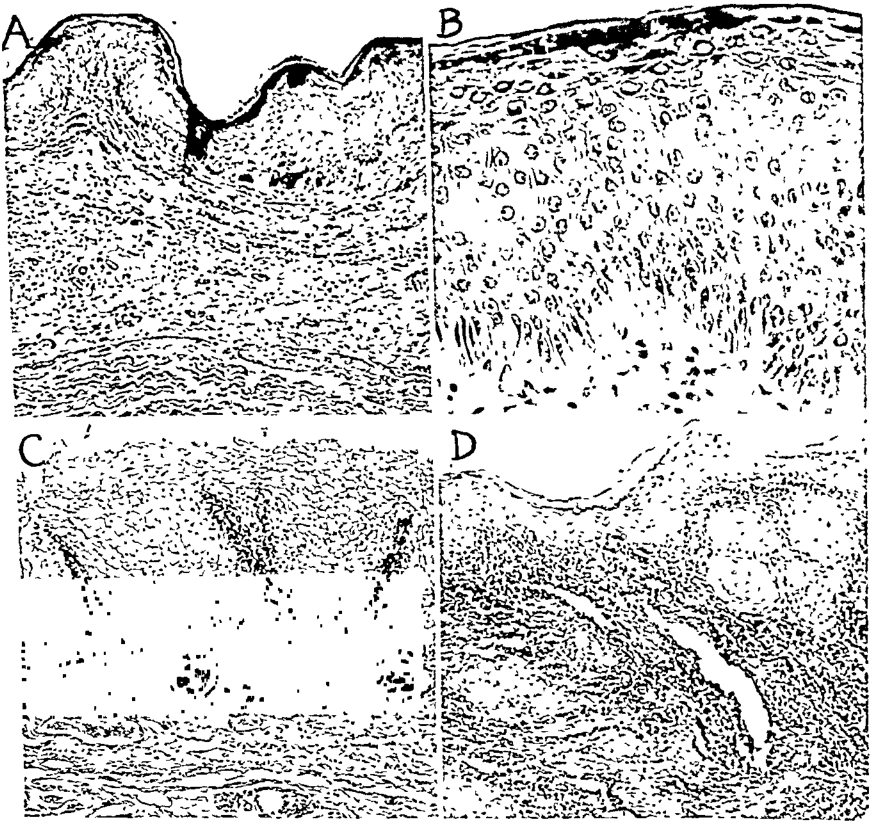

FIG. 1. *A*, leukoplakia of urinary bladder, × 50. *B*, leukoplakia of urinary bladder, × 215. *C*, stratified squamous epithelium lining urinary bladder, × 50. *D*, squamous cell epithelioma (grade 2 Broders' classification), keratinizing and infiltrating, associated with leukoplakia of urinary bladder. × 50.

4) Follow-up letters were sent to all patients known to be living. The questionnaires were made with a view of bringing the histories up to date.

The following results were then obtained under these three productive sections of the four projects.

Of the original 149 cases of leukoplakia of the urinary bladder, the diagnosis was confirmed by biopsy and tissue section in 45 cases, on the criteria previously set up. Undoubtedly, most of the other cases were true leukoplakias, but the diagnosis had been made by cystoscopy or at surgery and no biopsies taken or available, so they were excluded.

Of the 45 remaining cases, 32 occurred in males and 13 in females.

Of these original 45 patients with leukoplakia of the urinary bladder, 7 were proved beyond any doubt, by the available tissue sections, to have developed squamous epithelioma. This gave an incidence of 15.5 per cent for this series of proved cases.

Four of these patients were dead at this time and three survived.

Letters received in answer to my questionnaire from relatives of two other patients stated definitely that they had died of cancer of the urinary bladder, but in these 2 cases, no tissue was available to confirm the diagnosis. Seven patients had also died of causes other than cancer.

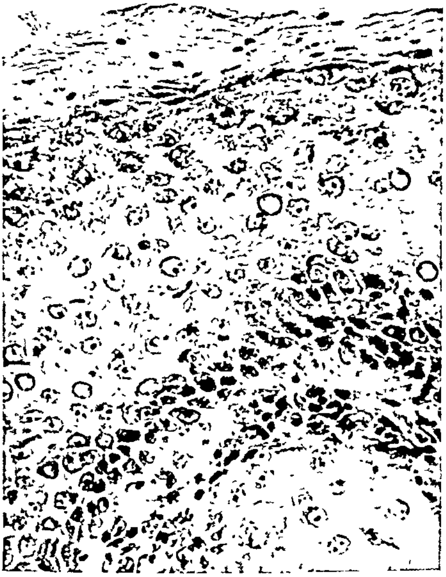

FIG. 2. Squamous cell epithelioma (grade 2 Broders' classification) keratinizing and infiltrating, associated with leukoplakia of urinary bladder, × 215.

If the word of the patient's relatives were accepted, the incident in this series would be 20 per cent, which figure is in agreement with the findings of most investigators of this lesion in other parts of the body.

Of the 7 cases of carcinoma, six occurred in males and one in a female who had a grade 1 papillary squamous cell epithelioma, Broders' classification.

Of the 6 cases in males, five were classified by Broders' classification: two, grade 2; three, grade 3. Table 1 illustrates this point.

Note that all these were squamous cell, keratinizing, and infiltrating tumors. Grading in squamous cell tumors means little or nothing. All squamous cell tumors are infiltrating and as vicious in character as can be found and with the exception of adenocarcinomas of the bladder have no equal.

The age incidence of carcinoma of the urinary bladder associated with leukoplakia was greatest in the 50 to 60 age group, there being four cases, but was almost equalled by the next decade with three cases in this group. This is illustrated in table 2.

These figures run parallel with the incidence of leukoplakia alone, which was greatest in the 50–60 group. Sixteen of the 45 patients were in this decade. Those in the 60–70 group followed with 11 cases. The youngest patient was 23 years old and the oldest 79 years of age. Table 3 illustrates these figures.

Studies of the laboratory findings revealed that 40 of these 45 patients, 88.8 per cent, had pyuria. Of these, 55.5 per cent had a definite upper urinary tract infection. These infections were all of long standing and are in complete agreement with the writings of Melicow.[10]

Urine cultures were found in thirty-one of the 45 cases. They were not at all conclusive in fixing the responsibility on any one organism. Streptococcus fecalis was found in 11 cases, and E. coli was found 9 times, a total of 20 out of the 31 cultures.

Syphilis, which in the past has been mentioned principally by French writers as a precursor of leukoplakia, was found in only 2 of these 45 cases, or 4.4 per cent, which is no higher than the incidence of syphilis found in the general population.

Our questionnaire was answered by 14 living patients; 7 reported themselves as well and without further trouble, while the other 7 reported severe vesical symptoms. This morbidity of 50 per cent might well indicate an increasing incidence of neoplastic changes.

I found 8 cases of leukoplakia in the 100 cases in which the bladder was claimed to be normal on gross examination. This was a surprisingly high incidence, but it was definitely found in the tissue sections of these 8 cases, or an incidence of 8 per cent. One infers that this diagnosis is frequently missed in the gross examination by the cystoscope.

DISCUSSION

In the short time alloted one could not hope to review etiology, symptoms, diagnoses, and treatment, and I shall only briefly mention a few high points.

Certainly, the most important factor in etiology is chronic infection, usually in the form of pyelonephritis. One must also note its occurrence in the aseptic bladders of males with benign prostatic hypertrophy and retention of urine, as noted by Patch and Rhea.[11]

Montgomery, Counseller and Craig[12] have shown that section of the pudendal nerve in patients with leukoplakia of the vulvae associated with puritis vulvae has caused complete remission and involution. This is another incidence of this lesion in the absence of bacterial infection and in the presence of only chronic irritation.

Patch and Rhea[11] have given us illustrations of the many changes that the mucosae of the urinary bladder may undergo. The following graph illustrates these changes as I picture them to their ultimate change or metaplasia.

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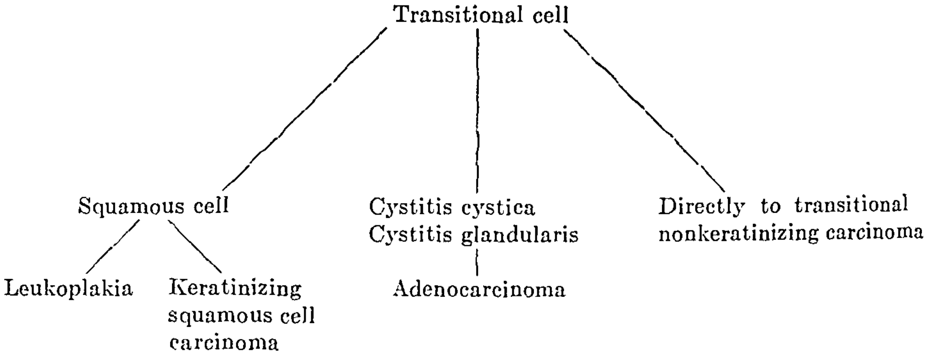
[10] Melicow, M. M.: Tumors of the urinary drainage tract. J. Urol., 54: 186–193, 1945.

[11] Patch, F. S. and Rhea, S. J.: Genesis and development of Brunn's nests and their relation to primary adenocarcinoma. Canad. Med. Assoc. J., 33: 597–606, 1935.

[12] Montgomery, H., Counseller, V. S. and Craig, W. McK.: Kraurosis, leukoplakia and puritis vulvae. Arch. Dermat. & Syph., 30: 80–100, 1934.



In the cases of congenital exstrophy of the bladder in which both the factors of mechanical irritation and bacterial infection are present it is not at all unusual to see leukoplakia, cystitis cystica, and cystitis glandularis all co-existing. The high incidence of malignant degeneration associated with exstrophy of the bladder has long been recognized and all types of vesical carcinoma, transitional, squamous, and adenocarcinoma are found.

In the differential diagnosis of leukoplakia one encounters no difficulty whatsoever with tissue sections. Grossly, incrusted alkaline cystitis may possibly be mistaken for leukoplakia because of its grayish or whitish appearance due to the deposition of calcium salts on the vesical mucosa.

In malakaplakia there are Michaelis-Gutmann bodies, which are calcium phosphate inclusion bodies in the larger myelotic cells of the mucosa. It may conceivably be mistaken for leukoplakia.

Yeast infections of the urinary bladder have been reported. They are very whitish in appearance. They are diagnosed by culture of yeast cells.

The treatment of choice today is fulguration of all vestiges of the lesion transurethrally or suprapubically if necessary.

Infection must be eradicated. Obstruction, retention, and stones are factors essential to eliminate for permanent cure.

Wolbach[13] states that leukoplakia is the effect of increased defensive proliferation of epithelium, the response of what might be termed the law of epithelium. He showed that 20 per cent of experimental rats on vitamin A deficiency diets died of obstruction by desquamating epithelium. Therefore, vitamin A in adequate dosage should be given these patients.

The use of cod liver oil locally and androgens have been used with reported successes, but there is insufficient evidence to include these in our armamentarium.

CONCLUSION

In conclusion, leukoplakia of the urinary bladder per se cannot be considered a precursor of carcinoma. The cells which are leukoplakic go normally on to their physiologic death. It is, however, found in association with carcinoma in sufficiently high incidence (15.5 to 20 per cent), to be quite alarming and would indicate that the same processes, or carcinogenic agents which cause one condition are responsible for the other. The most apparent single factor in this study was long-standing urinary tract infection, but it occurs in the aseptic bladder and in other parts of the body where mechanical irritation is the factor noted.

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[13] Wolbach, S. B.: Quoting Patch, F. S.: Leukoplakia and its association with squamous cell epithelium. New Eng. J. Med., **200:** 423–437, 1929.

It is not my intention to incriminate chronic infection as the sole cause of carcinoma of the urinary bladder associated with leukoplakia, but it does appear as an essential factor in the chain of events.

Block[14] stated the situation very well when he said that "until we know the biochemistry which characterizes the individual cell, we cannot give an unequivocal answer."

SUMMARY

In summary, 45 cases of leukoplakia of the urinary bladder have been studied. Thirty-two (71.1 per cent) of the cases occurred in males, and 13 (28.9 per cent) in females. Of these, 7 (15.5 per cent) have been proved subsequently to have had carcinoma of the urinary bladder. In 2 additional cases this diagnosis has been listed as the cause of death on the death certificates, but could not be confirmed. If these were accepted, the incidence would be 20 per cent in this series of cases.

It occurred in 6 males (85.7 per cent) and 1 female (14.2 per cent) and if the other 2 cases were included, the ratio is still higher: 8 males (88.8 per cent) and 1 female (12.2 per cent).

Pyuria occurred in 88.8 per cent of the 45 cases and upper urinary tract infection was established in 55.5 per cent. All types of organisms were found but Streptococcus fecalis accounted for 24.4 per cent of the infections.

Syphilis, which in the past has been considered of importance as a precursor of leukoplakia, was found to have no basis for this claim in this series; it was found in only 4.4 per cent.

Leukoplakia of the urinary bladder was found to be most common in the fifth decade of life while carcinoma associated with leukoplakia occurred almost equally in the fifth and sixth decades. The ratio of leukoplakia in males to females is 3 to 1, while in carcinoma associated with leukoplakia it is males 6 to 1, proved, and probably, 8 to 1.

The diagnosis will be made more frequently with the more frequent use of staining the urinary sediment, with the finding of epithelial pearls.

With the use of antibiotics and sulfa drugs, the incidence of leukoplakia of the urinary bladder should definitely decrease, and with it a lessening of malignancy associated with it.

The diagnosis must always be confirmed by biopsy. By so doing, the associated carcinoma will be discovered and eliminated when possible.

Cases of leukoplakia should be treated as potentially malignant and carefully followed, as we do our bladder carcinomas.

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[14] Block, B.: Cancers and precancerous affections from dermatological viewpoint. Cancer Rev., 7: 5–98, 1932.

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THE HEAT FACTOR AS A CAUSE OF HEMOGLOBINEMIA IN TRANSURETHRAL RESECTIONS

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Hemoglobinemia occurring during or following transurethral resections has been recognized by many investigators. The many theories and facts already set forth in voluminous literature led us to the realization that perhaps the real basic cause of hemoglobinemia remains unanswered.

The investigation of the effects of heat which is generated during usual transurethral resections has been carried out at our hospital since August 1950. Estimation was made of the total amount of calories developed during the operation; the amount of heat necessary to lake oxalated blood was determined and the development of hemoglobinemia due to the heat factor was studied and recorded.

Of historical interest, Schultz in 1865 observed degenerative changes in red blood cells on a heated microscopic stage. Hemoglobin in the renal tubules after severe burns was demonstrated by Ponfick in 1876 and by Fraenkel in 1889. Wilms in 1901 and Marchand in 1908 also noted these degenerative changes in the tubules. These two workers agreed that the changes were due to excretion of hemoglobin. More recently Christophe asserted that there is a toxic principle in the blood returning from the burned area. This observation was made on clinical and autopsy studies of 104 burned dogs. In 1947, Martineau and Hartman studied the effects of burns in 84 dogs and 20 humans. They believe that shock and intravascular hemolysis are the two principal pathologic-physiologic mechanisms causing this damage. The frequency of intravascular hemolysis in the presence of extensive cutaneous burns has been demonstrated. Yuile, Gold and Hinds in 1945 showed that the precipitation of hemoglobin in the renal tubules is primarily dependent on prior damage to the tubules, and not on the acidity or alkalinity of the urine or the amount of hemoglobin in the blood.

The level of hemoglobinemia varies widely from case to case and from report to report. The amount of free hemoglobin liberated cannot be correlated with the clinical symptoms. The similarity of the clinical picture in post-resection oliguria is pertinent to that seen with hemoglobinemia found in blackwater fever, incompatible blood transfusion, paroxysmal hemoglobinemia and in severe burns. Even minute amounts of hemoglobin in the plasma are known to produce vasoconstriction in the kidneys without being precipitated in the tubules.

Creevy and others attribute hemoglobinemia to the entrance of irrigating water into the prostatic veins and it thereby hemolyzes red blood cells. Several investigators have reported no hemolytic reactions since using glucose irrigating solutions. These important contributions toward solving this problem cannot be disregarded. Their experiments were sound and well controlled. However, we must look elsewhere for a complete solution of the cause of hemoglobinemia.

Landsteiner and Finch in 1947 demonstrated blood hemochromogen levels after operation to be between 24 and 316 mg. per 100 cc. They postulated at least two possibilities as to the cause of hemolysis: 1) local action of the electric energy of the instrument—experiments along this line were not carried out, and 2) penetration of the irrigating fluid into the blood stream. It has been found that 500 cc or more distilled water was needed to produce hemoglobinuria. Krumbhaar found in experiments on dogs that the intravenous injection of distilled water of 2 to 3 per cent of the body weight produced hemoglobinemia and hemoglobinuria. The speed of the injection had little effect on the amount of hemolysis.

In the course of an extensive series of experiments on shock, Kabat and Levine noted that a small proportion of the animals succumbed with extreme rapidity within a few minutes of burning. Since the sudden death in these experiments could not be explained on the basis of loss of fluid and since the nervous factor had been eliminated experimentally, the phenomenon was attributed to a toxin. The investigation was carried forward to study the possibility that changes produced by heat in the circulating blood could account for rapid death from burns. These workers believe that the fine precipitate of fibrinogen in heated plasma possesses the toxic properties. They further demonstrated that the particle size rather than the chemical constitution of this material bears the toxic properties. These findings show further proof that the picture of hemoglobinemia and hemoglobinuria is far from being a clear one.

In our experiments, the Bovie® Electrosurgical Unit, Model AG was used. This unit has a nominal frequency of 1000 kilocycles. The maximum power output varies between 275 and 300 watts, depending on the load resistances in use and also the individual measuring methods. Voltage output varies with the load being used. The AG Bovie output ranges between 2000 volts peak under the average cutting load to a maximum of 2800 volts peak at no load, when the dial setting is at 100 and the hemostatic control on step 2.

In the establishment of standards in the experiments, the method used may be referred to as elementary calorimetry involving "the method of mixtures." The basic principle is predicated on the assumption that no heat energy is gained or lost by the calorimeter can and its contents except that amount which is supplied by the cutting instrument. In the actual measurement, the instrument is operated within the calorimeter can, under conditions simulating actual operating conditions for a measured time interval, and the rise in temperature (in degrees Centigrade) of the can and its contents is noted. Since the gram-calorie is defined roughly as that amount of heat energy which is absorbed by one gram of pure water when its temperature rises one degree Centigrade, and since the specific heat of a substance is defined as the ratio of its thermal capacity to that of water, it follows that the heat absorbed by each body (can, solution, thermometer, cutting instrument) is simply the product of its mass by its specific heat by its temperature rise. Hence, the basic formula is:

$$H = (m_s c_s + m_c c_c + m_t c_t + m_i c_i)\Delta t$$

Where H is the total heat supplied by the machine, the m's are the several

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masses (or weights), the c's are the specific heats, Δt is the temperature change noted, and the subscripts identify the several bodies involved. Using this formula, the heat liberated by the electrosurgical unit per unit of time was determined.

Blood, plasma, saline, distilled water and 4 per cent glucose in water were used in the calorimeter. They were tested individually and also while containing tissues such as beef and human prostate. The dial settings were kept within the realm of our routine work. It was found that when the cutting load was set at 55 and the coagulation placed at 60 with the hemostatic control on step 2, the number of calories per second liberated by each type of current was 35.55. It is estimated that the source of error is roughly plus or minus 5.

There are two possible sources of error in the experiments which should be mentioned. First, the measurement of time of actual exposure of the current during the transurethral resections was determined by stop-watch. This method allowed for a human error. Second, the obtaining of blood specimens, although drawn by the same individual, constituted another source of possible discrepancy in our results.

The following method in obtaining the blood samples was used. Test tubes, syringes and needles were clean and free from moisture. Ten cc. whole blood was withdrawn from the vein with extreme care so as to prevent breaking down of cells. This was placed in a tube containing 5 drops of heparin. The tubes were stoppered and centrifuged as soon as possible. The plasma was then removed for further examination. Plasma hemoglobin determinations were made using the "cyanmethemoglobin method for measuring hemoglobin" recommended in the Symposium on Hemoglobin conducted by the American Society of Clinical Pathologists. This method uses the principle of laking blood with water and converting the hemoglobin to cyanmethemoglobin. The concentration of cyanmethomoglobin is measured in either a visual or photo-electric colorimeter. The mixed cyanide reagent consists of 3 gm. of potassium ferricyanide and 1 gm. of potassium cyanide dissolved in water and diluted to one liter. A green filter is used. When 0.4 cc plasma, 5 cc water, and 0.1 cc cyanide solution are mixed, the conversion of hemoglobin to cyanmethemoglobin occurs immediately. Hemoglobin as such is read directly from the calibration curve which had been plotted previously. All determinations of plasma hemoglobin in our study were made by using the Hellige-Diller Photoelectric Colorimeter.

Eleven patients were used as controls. They were chosen on the basis of having minor ailments or completing postoperative care. Samples of blood were obtained every 2 hours over a 6 hour period. Food and liquids were allowed during this time. Two patients showed lipemia in some samples, therefore they are not included in the results. The remaining 9 cases showed an average 0.8 mg. per cent change in plasma hemoglobin. The highest change was 2.2 and the lowest zero.

Four healthy dogs were also used in our studies. The first dog was given distilled water subcutaneously. Total amount given over a two hour period was 2200 cc. Within the first 10 minutes, the dog received slightly more than 3 per cent of its body weight. The hemoglobin levels in the plasma increased at a regular rate. During the 2 hours the plasma hemoglobin increased 40 mg. per cent (fig. 1).

Three dogs were subjected to electrosurgical resection of the vesical neck. One experiment was unsuccessful due to technical difficulties. The other two dogs were subjected to routine resection through a suprapubic route. Four per cent glucose solution was used for irrigation. The plasma hemoglobin increased in proportion to the number of calories applied. The average increase of plasma hemoglobin was 446.5 mg. per cent

Autopsy specimens revealed variable findings. The dog receiving distilled water showed definite evidence of water intoxication. The lungs revealed marked congestion in the capillaries in the alveolar walls. Arterioles occasionally presented early fibrin deposits near the intima in which some leukocytes were enmeshed, but there was no evidence of organization and no distinct thrombosis. Bronchioles and alveoli were universally empty. There was no pigment deposition.

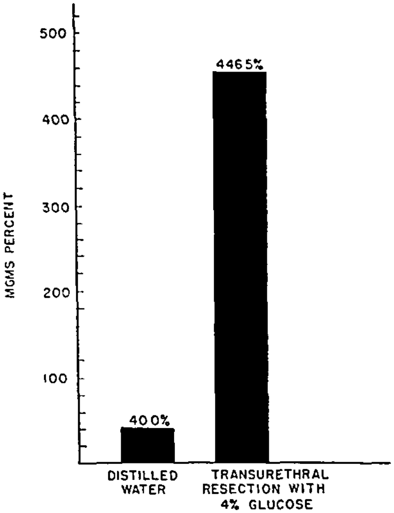

FIG. 1. Change in plasma hemoglobin

The heart and spleen showed no changes. The liver revealed marked congestion of the centrolobular areas. The cords of hepatic cells stained poorly. The nuclei also stained poorly and the cytoplasm was pale and some times frayed.

The kidneys revealed marked congestion in the glomerular capillaries and capillaries between the tubules. The glomeruli showed no increase in cellularity, inflammatory reaction or adhesions. The glomerular spaces were empty. The proximal tubules presented swelling, granularity and fraying of epithelial cells resembling cloudy swelling. The tubules otherwise showed no abnormality and were empty. No pigment, granular or cellular casts were seen.

The dogs, undergoing resection of the vesical neck with glucose solution for irrigation, showed marked pulmonary edema and congestion. The alveoli and bronchioles generally showed marked serous transudation. The capillaries and arterioles were markedly congested with intact erythrocytes. Several large arteries were filled with fibrin thrombi. The liver and spleen were within normal limits.

The kidneys had focal tubular lesions. No abnormalities were seen in the glomeruli, but there were focal collections of lymphocytes with occasional plasma cells occurring around several proximal tubules. There was some tubular enlargement and piling-up of cells with dark nuclei and an occasional mitosis. The prostate showed fulguration effect; otherwise, there was no lesion. The urinary bladder revealed marked congestion of all the vessels but no definite pathological changes were noted.

Although the pathological lesions are not conclusive, they represent some changes which were found by investigators who studied the effects of burns.

Simple inspection of the plasma or serum usually does not forewarn us as to impending hemoglobinemia. Ten cases were studied by the qualitative method. None of these showed the visual presence of hemoglobin. The highest level of plasma hemoglobin was 32 mg. per cent on quantitative determination. This could not be detected as free hemoglobin by simple visual inspection. It is quite obvious that more information, especially as to prognosis, can be derived by the quantitative method.

It is interesting to note that only 10 per cent of the total time required to complete a transurethral resection was actually used in cutting and coagulation.

Fifty cases of prostatic resections were studied to determine the number of calories produced during the operations. The plasma hemoglobin was determined quantitatively before, during and after resection. The shortest operation produced 1,990 calories and the longest showed 27,302 calories.

There was no selection of cases. The ages ranged between 51 and 76 years. No correlation could be found between the changes in plasma hemoglobin and age. Also the weight of the individual had no relationship to the amount of hemoglobinemia produced.

After determining the actual exposure time of the current, the calories were then computed. Five cases are included in the first group which is below 2500 calories. These averaged 3.7 mg. per cent change in plasma hemoglobin. Nine cases were in the 5,000 calories group and these averaged 6.1 mg. per cent changes. Between 5,000 and 10,000 calories there were 12 cases. These increased 8.15 mg. per cent on an average. Between 10,000 and 15,000 calories there were also 12 patients with an average increase of 10.8 mg. per cent. In the 15,000 to 20,000 group the greatest increase in plasma hemoglobin was detected. These 10 cases showed an average of 20.0 mg. per cent increase during the resection. There were only 2 cases receiving over 20,000 calories. They averaged 10.3 mg. per cent increase.

From these findings a graphic correlation between the number of calories produced and the amount of hemoglobinemia resulting from such heat can be made (fig. 2).

The sudden decline in plasma hemoglobin after 20,000 calories are produced cannot be explained fully. Of course, in this study only 2 cases are to be found in this group. This number is not sufficient to use as a correlation, but it was included to complete our study. One factor which should be considered is that
ulation produced by prolonged exposure and, thereby, decreasing the amount
tration.

The danger level appears to be between 15,000 and 20,000 calories. It is during this amount of exposure that the hemoglobinemia is most marked and shows the greatest increase. The danger zone appears to be after seven minutes of actual exposure to the current. Beyond this limit closer attention to the patient's condition should be given. Should any untoward reaction develop, the operation should be discontinued and completed at some future date.

It is hoped that these observations will stimulate further investigation into the heat factor as a cause of hemoglobinemia in transurethral resections. This concept may be the ultimate answer to this problem.

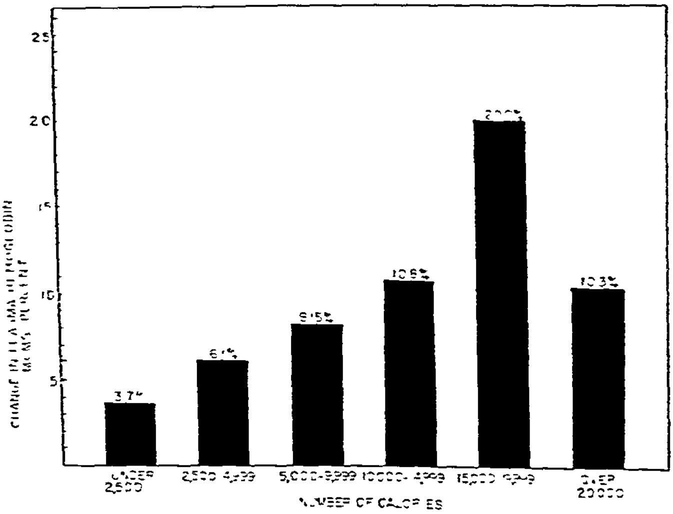

FIG. 2. Transurethral resection of prostate (50 cases). Four per cent glucose solution used.

SUMMARY

The effects of the heat generated during transurethral resections were investigated.

The total amount of calories developed during operation was estimated.

The amount of heat necessary to lake blood and the amount of hemoglobinemia developed by the heat factor during transurethral resection have been determined.

The heat factor must be recognized as an important phase in the solution to the problem of hemoglobinemia during transurethral resections.

It is suggested that high-frequency machines used in surgery be calibrated by their makers to show their caloric output per second at different settings.

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A STERILE, DISPOSABLE, PLASTIC, WATERPROOF DRAPE FOR TRANSURETHRAL SURGERY AND CYSTOSCOPIC PROCEDURES

GEORGE L. GARSKE

The inception of transurethral type prostatectomy initiated a new era in urological surgery. Since it was first devised, many improvements have been made in its method and techniques. We now have a very complete instrument armamentarium for this type of surgery, but even with all of the preciseness that speaks of urology, we are still operating in a relatively nonsterile field, simply because of our method of draping the patient and the operating table.

Most tables used for transurethral surgery have some type of a tray, and collecting screen which may, or may not, be sterilizable. Only a few of the tables have sterilizable elements, and these elements are necessarily cumbersome and difficult to handle for sterilization. Many times, because of this situation, they are not completely and thoroughly sterilized by boiling or autoclaving, but rather by solution immersions.

The method of draping the patient, and the material used for draping are in themselves precursors of a nonsterile operative field. All urologists are aware of the elements presented in draping the genital area, and there have been many individual variations for such draping because of these anatomical and physiological characteristics. The cotton and linen used for draping the genital and perineal area do not lend themselves satisfactorily to aseptic technique, chiefly, because of their absorptive qualities. They, therefore, cannot be efficient, or effective, barriers against the passage of contaminating organisms from the contiguous skin tissues, or structural materials of the table. If a linen or cotton towel, or drape, is applied to a dry, aseptically prepared area, the field is theoretically sterile. However, as soon as this area becomes soaked with water, even though the water may be sterile, the surgical field immediately becomes a nonsterile field because of the absorption by the drape from the nonsterile contiguous area.

In 1948, T. S. Gerspacher, et al.[1] conceived the idea of a disposable, waterproof, impermeable surgical drape made of a vinyl plastic material. The problem of limitation of a sterile field to a definite area was also considered, and it was conceived, and concluded, that a pressure sensitive adhesive coated area on the plastic drape would effectively seal the operative site, and hold it firmly in place without the use of towel clips, or other drape holding devices. This original project of a disposable, waterproof, plastic drape was further developed to a sterile package principle by which the nursing staff could obtain an easily stored, sterile package, open the package, this package still remaining sterile, and place it in immediate use.

Several trials were made with the standard available drapes of a large manufacturer of abrasives and adhesives,[2] and after considerable experience, the author devised the drape described in this paper. This drape, and the method in which it is used, should make transurethral surgery practically a sterile procedure, particularly by prevention of the possibility of contamination of skin bacteria, and, or, contamination from a nonsterile structure of the operating table by an impermeable, disposable, sterile, waterproof, plastic drape barrier.

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[1] Gerspacher, T. S., Fowler, H. D. Jr. and Rolf, D. E.: A. M. A. Arch. Opth., 45: 673–677, 1951.

MATERIAL

These drapes are made of a pleasant, restful, glare-reducing, green-colored, soft draping, thin vinyl plastic film which is nontoxic, inert, and unaffected by surgical solvents and detergents. This drape measures 32 by 50 inches, and at one end, approximately 12 inches from what will be termed the top of the drape and 16 inches from the sides of the drape, is a transverse orifice measuring approximately 3 by 2 inches in diameter with a 1¼ inch border of pressure sensitive adhesive (fig. 1). The plastic drapes are completely moisture-proof and will adhere to the skin upon contact at the site of the adhesive, forming an impermeable barrier to contamination. The light-weight plastic construction, and pressure sensitive adhesive permits it to conform to the irregular areas of the body, making it very easy to drape the anatomy necessarily encountered in transurethral surgery.

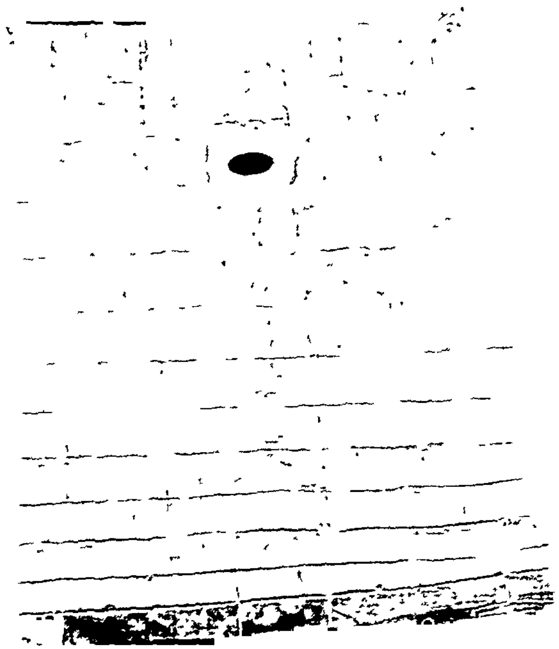

FIG. 1. View of unfolded drape

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[2] Minnesota Mining and Manufacturing Co. (Tape Division), St. Paul 6, Minn.

To assure sterility in the manufacture of these drapes, careful bacteriological studies were conducted by Dr. H. O. Halverson and his associates at the University of Illinois.[1] They designed a system of complex laboratory controls with heat resistent organisms such as P.A. 3679 and Bacillus stearothermophilus N.C.A. strain No. 1518 in order to insure absolute sterility.

The complete process begins with dusting each drape with surgical powder prior to folding. It is double wrapped in glassine paper, light blue colored paper next to the drape, and natural color over that. The fan-folded package is then inserted into a foil and film envelope. A special vinyl film provides the inside or sealing surface of this envelope. The envelope is then placed on an endless conveyor track which carries it through heaters and an automatic heat sealing unit. All the excess air is squeezed from the envelope before the envelope is sealed by knurled rollers.

Batches of the sealed envelopes are then steam autoclaved at 250F with 15 P.S.I. of saturated steam. Minimal autoclave cycles require that the exhaust steam temperature be at, or above, 250F for 40 minutes. Thermocouple readings are also taken from inside selected envelopes to insure that internal temperatures correspond to the exhaust temperature. Every autoclave load, approximately 1,000 drapes, is further checked for sterility by bacteriological methods. A percentage of the drapes in each batch are inoculated with an organism of known thermal death factor (Bacillus stearothermophilus N.C.A. strain No. 1518). These specially identified drapes are then placed in the autoclave and sterilized along with the rest of the batch. After the sterilizer is unloaded, the inoculated drape packages are tested and cultured for 96 hours at 131F to determine the efficiency of the sterilization cycle. The rest of the sterilized batch is placed in storage and marked "hold for bacteriology check." Only after a negative report is received on the batch are the stored drapes marked "released for distribution" by the bacteriologist responsible for sterility control. Individual drape packages and cartons are then marked with a sterilization report number and placed in shipping cartons.

TOXICITY AND SENSITIVITY STUDIES

The problem of skin and mucous membrane irritation and systemic injury in animals was studied by Love, Wright and Bieter[1] in the Department of Pharmacology at the University of Minnesota. The technique described was largely that described by Draize, Woodard and Calvery.[3] Briefly, the results of these investigators were as follows:

1) Adhesives used on surgical drapes of the vinyl plastic film which makes up the drape backings were applied to the shaved skin of albino rabbits for periods of time up to ninety days. In no instance was any irritation produced by the adhesive.

2) The same was true of the vinyl film if aeration beneath the test film was allowed by punching holes in the film. When a continuous film of vinyl sheeting

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[3] Draize, T. H., Woodard, G. and Calvery, H. O.: J. Pharm. and Exper. Therap., **82:** 377, 1944.

was held in close approximation with the rabbit skin, erythema and maceration of superficial tissues began to occur on the seventeenth day of the test. If at any time aeration was provided, the skin rapidly returned to normal. During these tests, no changes occurred in the blood or urine of the test animals, and weight gains for all animals were normal.

Four test substances were utilized in further studies: 1) surgical drape adhesive; 2) the vinyl film; 3) commercial adhesive plaster; and 4) a commercial adhesive plaster containing a fungicide, were applied to the skin on the inner forearm of each group of volunteers. In the separate tests for a single application for a duration of 48 hours, daily applications for 11 days, and 5 applications over 21 days, normal skin areas were observed (table 1). The reactions observed consisted of itching, erythema and exfoliation. When these materials were applied repeatedly, the reactions became more severe. Most of the volunteers could not tolerate the two adhesive plasters for more than 6 days. On the other hand, surgical drape adhesive was easily tolerated by all individuals for the duration of the test.

Clinical trials of the drapes were conducted on 349 patients undergoing various types of surgery and there was no evidence of skin or wound irritation noted in the entire series. In one group of 342 patients, the duration of application of the adhesives to the patients varied from 15 minutes to 4¾ hours, and in a few cases reapplications were made for a period of time from 2 to 4 weeks. In not a single instance was any evidence of irritation, or intolerance observed.

TABLE 1

	48 hrs.	*11 days*	*21 days*
Surgical drape adhesive	72%	92%	43%
Vinyl film	87	85	86
Commercial adhesive plaster	27	0	14
Commercial adhesive plaster (containing a fungicide)		8	

USE OF THE DRAPE FOR TRANSURETHRAL SURGERY OR CYSTOSCOPY

1) A 24 inch length of household type wax paper is placed beneath the patient's hips, letting it fall freely over the front of the table for one half its width (fig. 2, *A*).

2) Prepare the skin area in a routine manner and remove the excess fluid with sterile gloves and gauze to assure a completely dry skin area.

3) The pressure sensitive adhesive is then exposed by grasping, with a sterile gauze sponge, the free edge, or lip, of the protective paper liner covering the adhesive. The drape is then placed over the penis, or introitus, with the top of the drape toward the patient's head. The penis is brought through the transverse orifice and the pressure sensitive tape is approximated to either side of itself, around the penis, thus sealing off the penis from the remainder of the body.

4) The top part of the drape is then extended over the abdomen. The long bottom part is brought down, tucked beneath the buttocks and then draped over the tray on either side and also in front of the tray (fig. 2, *B*). This should be done

in such a manner so as to include sterile draping of the handle of the tray, so that the tray may be grasped with the handle in the drape without fear of contamination of the operator's sterile gloved hand.

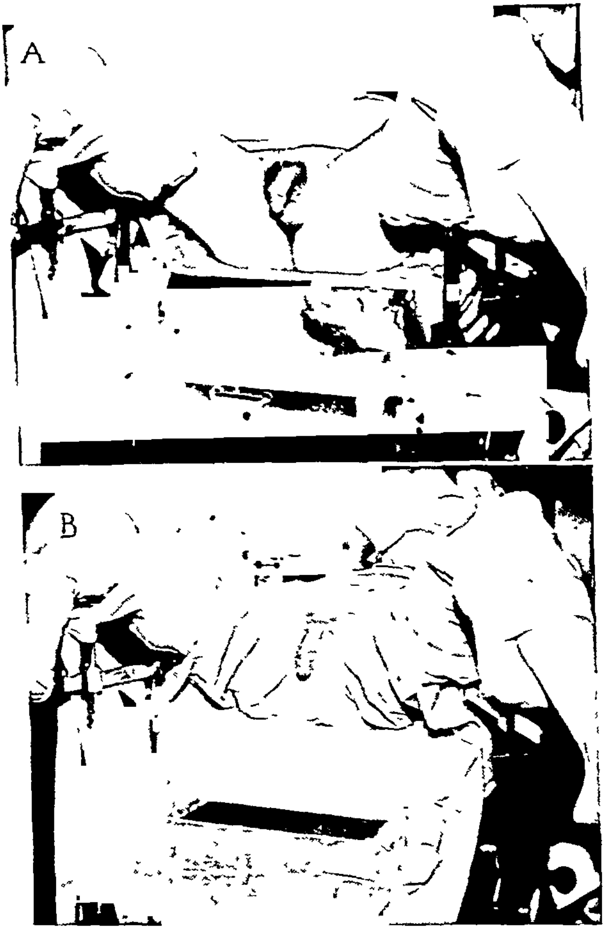

FIG. 2 *A*, patient in position for transurethral surgery on Sisk operating table. Note wax paper beneath buttocks. *B*, drape in place prior to completion of linen draping. Penis has been placed through transverse orifice in drape, and pressure sensitive adhesive has been approximated to penis, to adjacent skin, and to itself to effect watertight seal. Drape has been tucked beneath buttocks, and then brought down over front of butt end of operating table, and over tray. Sterilized screen tray has been put in place in main tray.

5) Autoclaved or steam sterilized screen trays are placed in the main tray and over the drape.

6) Sterile linen leggings are applied (fig. 3, *A*).

7) A transverse slit with a No. 15 scalpel blade or with sterile scissors is made in the drape on the floor of the tray at its junction at the butt end of the table so that the irrigation fluid may drain to the floor trap or collecting basins.

8) If the operator uses the rectal sheath of O'Conor, the rectum is localized and a cross cut of approximately 2 cm. is made over the rectum, and the rectal sheath inserted and affixed to the buttocks with four small towel clips (fig. 3, *B*).

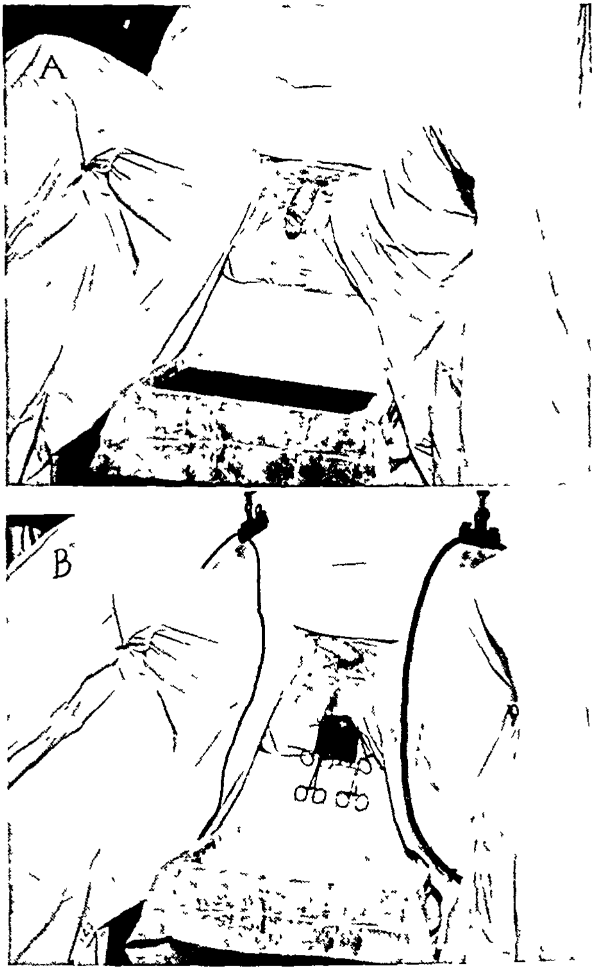

FIG. 3. *A*, linen leggings have been applied to legs, and sterile drape has been applied to upper field. Towel clips have been used to secure drape about legs, and upper field drape has been brought up over x-ray unit of Sisk table and secured with towel clips to effectively produce completely sterile field. *B*, rectal sheath in place and secured with small Backus towel clips directly to buttocks Note how lowermost towel clips have included medial finger fenestra of uppermost towel clips in their jaws.

9) The irrigation tubing, electrosurgical connection and the light cord are brought into the field in the usual manner of the operator.

This drape not only has a useful and practical purpose in transurethral surgery, but can be used for all male or female endoscopic procedures in the hospital and in the urologist's office.

SUMMARY

An economical, sterile, disposable, plastic, waterproof drape for use in transurethral surgery or cystoscopic examination is presented.

The drapes are nontoxic and inert in character.

The operative site is clearly demarcated and sealed off.

They are not absorptive in contrast to linen and cotton. Therefore, they act as effective barriers against passage of contaminating organisms from the skin surfaces or other foreign objects which are contiguous to the sterile field.

The drape is sterile indefinitely, and is easily stored and ready to use at notice.

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AN AUTOMATIC VALVE FOR USE WITH THE RESECTOSCOPE

LEO R. PRINS, JR.

Transurethral prostatic resection entails the well coordinated use of hands, feet and eyes. This is necessary to properly control the motions of the loop, the flow of current and the flow of irrigating solution. It is one of the reasons why the procedure is difficult to teach and terrifying to the beginner. Likewise, it is one of the reasons for the recent swing back toward open operations by many urologists. The device to be described was created with the idea of eliminating one of the many motions required of the resectionist.

The automatic valve is simply a non-corrosive ball (fig. 1) placed in the water inlet of the resectoscope sheath. The ball is lifted by small pins attached to the cones of the operating and examining elements used within the sheath. With the operating element or examining telescope in place, the fluid runs. Withdrawal or removal of the operating element or examining telescope automatically closes the valve.

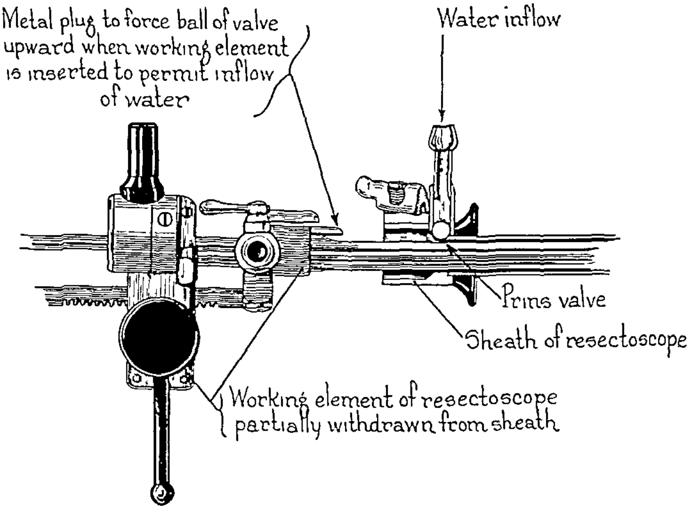
Metal plug to force ball of valve upward when working element is inserted to permit inflow of water
Water inflow
Prins valve
Sheath of resectoscope
Working element of resectoscope partially withdrawn from sheath

FIG. 1.

A second advantage in the use of this device is the virtual elimination of bubbles from the field. The reason is not clear but the fact remains that troublesome bubbles do not obscure vision when this valve is in use.

If it is desirable to shut off the fluid for inspection or search for bleeding points this is easily done by compression of the tubing at its point of attachment to the water inlet.

The device does simplify transurethral resection in some degree, saves time and temper and is a useful aid in a highly technical and often very trying procedure. It is adaptable to most types of operating elements.

I wish to express my thanks to Mr. Kenneth Nelson of Albert Lea, Minnesota, who made the first working model and to Mr. Frederick Wallace of American Cystoscope Makers, Inc. who has brought the instrument to its present fine state.

222 Medical Arts Bldg., Albert Lea, Minn.

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PERINEAL SURGERY IN CARCINOMA OF PROSTATE

DANIEL R. HIGBEE

No more challenging problem confronts urologists than the cure of carcinoma of the prostate.

When we consider its frequent incidence, its silent progress in the early stages, and its almost uniformly fatal termination, little progress is being made in the number of cures obtained.

Brilliant as have been the research discoveries which have done so much to prolong the life and comfort of the prostatic patient with carcinoma, these still leave us short of our objective, and in the end, carcinoma is still nearly 100 per cent fatal.

Until other methods of cure are discovered, total surgical removal alone offers any chance of cure. But we find urologists, as a whole, not sufficiently convinced of its worth and not sufficiently interested to have equipped themselves with the ability to offer cure when cure may be expected.

This attitude may be justified in part by the advanced age of many of the patients, who have a limited life expectancy under any circumstances, by the great benefit offered by modern palliative treatment, and by the number of cases of failure where total surgical removal has been employed. However, improvement in our results, if we are to cure more of these patients and give the uncured a longer life expectancy, would seem to lie in a wide dissemination to the public of the value of routine rectal examination in men past fifty; in a more deliberate and critical appraisal of the prostate before any surgical procedure is employed; in more of us equipping ourselves with the technical ability to remove the earlier malignancies; in further study of the value of subtotal prostatectomy and perhaps the use of both palliative therapy and perineal surgery in more of the borderline cases.

As some of you are aware, I have been interested in perineal surgery for a number of years. This interest has come from, first, a desire to be able to remove carcinoma of the prostate surgically where indicated and, second, a wish to utilize more routinely a method of prostatic surgery in other cases, carrying little risk to life, few complications, and yielding good end results.

In the course of thus treating 572 cases of prostatic obstruction by perineal surgery, up to January 1, 1951, there have been 10 deaths, a mortality rate of 1.75 per cent; morbidity has remained approximately 8 per cent, and end results have compared favorably with other methods. Of this number, 36 patients have been treated for carcinoma of the prostate by perineal surgery. These 36 from a total of 155 cases of prostatic carcinoma seen during the period under consideration constitute 19 per cent.

PATHOLOGICAL DATA

The view often expressed that the posterior lamella of the prostate gives rise to carcinoma is to me a misnomer. From an embryological standpoint the prostate

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Presidential address read at annual meeting, South Central Section, American Urological Association, Houston, Texas, October 30, 1951.

develops from two separate and distinct groups of glands. The short rudimentary ones arising from the floor of the urethra characteristically give rise to extensive hyperplasia but rarely to malignancy. These are separated from the more complex glands which make up the anterior lateral and posterior lobes of the adult prostate by a thin fibrous capsule. As adenomatous changes develop, this glandular tissue of the prostate is often flattened or compressed against the outer capsule. Malignancy is prone to develop in these glands of true prostatic tissue and in any part of it, as the work of Kahler[1] in reviewing 195 cases of prostatic malignancy at the Mayo Clinic has shown. In Kahler's series, localized lesions were present in 96 cases, 6 in the anterior lobe, 46 in the lateral lobes and 44 in the posterior lobe; 16 per cent arose in areas of nodular hyperplasia.

Early malignancy is very often palpable far out in one or the other of the lateral lobes, more often I believe in a lateral location than in the posterior lobe itself.

In this group of cases the primary site of malignant change seems to have started in, or have been confined to a lateral or posterior lateral area of the prostate in 10 of the 17 cases in which the malignancy was still confined to the prostate itself, and to have progressed beyond the stage where the original site could be determined in the remaining 26.

DIAGNOSIS

In operating upon a considerable number of patients, it is not surprising that errors in diagnosis might occasionally occur, and, in this group, 5 individuals were treated by total perineal prostatectomy, but microscopic examination of the tissue removed failed to show any evidence of malignancy.

Also, as you may surmise, some cases in which malignancy was not suspected preoperatively proved, upon operation and examination of the tissue, to be malignant. There were also a few cases in which hypertrophy and malignancy were associated and which were treated by simple perineal prostatectomy from choice. This group, composed of 9 cases, will be discussed later. This fact naturally brings up the question of the advisability and value of biopsy by frozen section at the time of surgery.

There are two good reasons for resorting to biopsy. First, a positive diagnosis may be established by sampling an area of doubtful hardness and one may then proceed with the total removal of the gland without uncertainty; or a patient may not wish to consent to radical removal unless the diagnosis has been first definitely established by frozen section.

There are also several reasons for *not* performing a biopsy. The biopsy may prove to be incorrect, having been taken from the wrong area, or to have been inadequate in amount. There is also the possible danger of contaminating the surgical field even though the incised area is closed by sutures, particularly when the operative procedure to follow may be attended by considerable manipulation of the gland.

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[1] Kahler, J. E.: Carcinoma of prostate gland: A pathological study. J. Urol., 41: 557–574, 1939.

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In this series, biopsy by frozen section was resorted to at the time of operation in 12 instances. Nine of these corresponded with the later microscopic examination of the tissue removed; three did not. In other words, in 3 operable cases of malignancy of the prostate the patients were treated by conservative prostatectomy instead of total, because the biopsy failed to prove the true nature of the underlying disease.

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[1] Kahler, J. E.: Carcinoma of prostate gland: A pathological study. J. Urol., 41: 557–574, 1939.

Of the 9 cases in which the biopsy did agree with the findings at operation, six confirmed the presence of malignancy; three showed no evidence of it, so that a conservative procedure was substituted.

In order to minimize such errors, the writer believes from the aforementioned experiences and from the pathological data already cited, that if a biopsy is to be taken, a relatively wide and deep section should be removed from the suspected area. It should include tissue well back toward the base of the prostate, as palpation over a gland adequately prepared for operation by estrogen therapy often fails to identify a characteristically hard area, and one must at such times rely on his interpretation of the extent and location of the malignancy prior to the time such therapy was instituted. This may have been from one to three weeks earlier.

While the diagnosis of prostatic malignancy by rectal examination is approximately 85 per cent accurate, this accuracy depends somewhat on the stage of development in which the carcinoma is found and upon the subsequent rate of growth. The latter is variable and may be slow or rapid.

Three of these patients were observed in whom there was a small hard area in one lobe of the prostate, unchanged over a period of 2 years. These proved to be malignant at the time of operation and should have been assumed to be malignant and removed earlier had this been possible.

On the other hand, one patient, a physician, was examined one year previous to his operation and found to have a normal small soft prostate. One year later at the time of operation, the gland was large, hard, malignant, and weighed 100 gm.

It is therefore my belief that any prostate showing a localized area of hardness, persisting over 3 months' time and not associated with calcium deposits or infection, should be assumed to be malignant and totally removed, the patient's age and general condition permitting. Few errors will result from such decisions.

PROCEDURE AND TECHNIQUE

From the standpoint of procedure and technique, those interested are referred to techniques described by the Johns Hopkins group,[2] Belt[3] and others. However, there are certain considerations which are both interesting and important. Good position during operation is absolutely necessary. A blood transfusion during a procedure which may last on the average of from 1¼ to 1¾ hours and in which blood loss cannot always be immediately controlled, is very helpful in maintaining the good circulatory and general condition of the patient, and I now use it almost routinely.

[2] Young, H. H.: Cure of cancer of prostate by radical perineal prostatectomy (prostatoseminal vesiculectomy); history, literature and statistics of Young's operation. J. Urol., **53:** 188–252, 1944.

[3] Belt, E., Ebert, C. E. and Surber, A. C. Jr.: A new anatomic approach in perineal prostatectomy. J. Urol., **41:** 482–497, 1939.

While the peri-anal incision is supposed by some to give inadequate exposure, with a consequent multiplication of difficulties, my experience has not borne this out. I use it routinely and believe there is less disturbance to the region of the perineal body and thus greater assurance of preserving good urinary control than by the wide incision into each ischiorectal fossa with posterior reflection of the levator ani muscle.

It has seemed to me a sounder surgical procedure to incise the posterior fascia overlying the vesicles, to strip the rectum well away posteriorly and to delay the complete delivery of the vesicles until after the prostate has been excised from the vesical neck, thus removing the prostate and the vesicles as a block dissection rather than to attempt to deliver the vesicles completely before the prostate has been so excised. In this way extension into tissue adjacent to the prostate with the accompanying lymphatics may be included which otherwise might be left behind.

In anastomosing the urethra and vesical neck it is very helpful to leave just enough prostatic urethra to suture easily to the bladder, and contrary to some techniques described and illustrations in textbooks, it seems more logical to me to obtain a good anastomosis, urethra to bladder after first reducing the bladder neck in size by anterior and lateral reduction sutures, rather than to reduce the bladder neck after anastomosing the superior edge of the urethra with the roof of the bladder. In some techniques this allows the trigone to fall back well behind the site of anastomosis. This method leaves the fixed part of the bladder undisturbed and sutured directly to the urethra which is also fixed in its position by the triangular ligament and perineal body. At least the technique described above has been followed, and no postoperative strictures have developed.

PREOPERATIVE CARE

All patients were prepared by estrogen therapy in moderate dosage for from 10 days' to 3 weeks' time. Patients not tolerating ethinyl estradiol were switched to stilbestrol and vice versa, depending upon their tolerance. In 70 per cent of the cases of carcinoma there was a marked reduction in size and a softening of the gland. In 20 per cent there was moderate reduction in size and in 10 per cent there was no appreciable change.

In cases where fixation to the pelvic fascia seemed to exist, the response to estrogens was used primarily as a test in determining operability. All patients were given preoperative catheter drainage and antibiotics for from 5 to 9 days.

Preoperative acid phosphatase determinations were within normal limits in all but one instance and in this case a determination of 4 mg. per cent was considered to be inconsistent with the clinical findings and the patient has remained apparently well for 2 years and until the present time.

MORTALITY

There was one mortality, a rate of 3 per cent, a sudden massive pulmonary embolism on the third postoperative day. In this instance the prostate contained a large stone and an abscess in addition to the carcinoma.

COMPLICATIONS

In seven of the 36 cases complications developed. Four were pleuritic or embolic, one had phlebitis and two had urticarial reactions to the estrogens.

The postoperative hospital stay varied from 12 to 30 days, 15 patients being discharged in 14 days. One rectal injury healed within 3 weeks' time. Prolonged urinary fistulas did not develop in any case. The longest period of incontinence occurred in the first patient operated upon. This lasted 4 months but the patient eventually obtained complete urinary control. One other patient would have had permanent incontinence had he survived his convalescent period, but he died a violent death 2 months postoperatively. In this instance a small portion of the urethra was evulsed with the apex of the prostate at the time of surgery.

One patient has slight incontinence if he wears a truss or a tight abdominal belt but has adequate urinary control without these.

Sixteen patients had complete urinary control from the beginning and the remainder gained normal urinary control within a few weeks to two months' time. None have developed strictures requiring urethral dilatations.

ANALYSIS OF CASES

The 36 cases comprising this report will be considered in four groups: Five cases of adenomatous hyperplasia were treated by radical surgery. Nine cases of carcinoma of the prostate were treated by conservative enucleation, castration, and estrogen therapy. Five cases of carcinoma of the prostate were treated by radical surgery plus castration and estrogen therapy. Seventeen cases of carcinoma of the prostate were treated by radical surgery only.

Group 1. There was recovery in all 5 cases of adenomatous hypertrophy treated by radical surgery in which no evidence of malignancy was discovered on pathological examination and all have good end results. These glands were either hard, irregular, or somewhat asymmetrical on palpation; and on pathological examination showed considerable fibrosis and/or infection present in addition to the hyperplasia. It is perhaps noteworthy that these cases showed little or no response to estrogen treatment and biopsies might well have been employed, and which I believe should be employed in those cases which do not show response to estrogens unless one is reasonably sure of the diagnosis.

Group 2. In 9 cases of carcinoma of the prostate treatment was by conservative enucleation, castration, and estrogen therapy. Of these, malignancy was unsuspected in 3 until the pathological report was returned. The biopsy report was incorrect in 3; and in 3 enucleation plus castration was carried out as the treatment of choice in 3 poor risk patients. Bilateral orchiectomy was performed on all at the time of or soon after the initial surgery.

Of this group 4 are dead. One died 2 months postoperatively of a sudden cardiac infarct. One died of diabetes, hypertension, and malignancy 2 years after his operation. One died 5 years postoperatively following a broken shoulder complicated by pneumonia and 1 patient could not be contacted 5 years postoperatively and is considered dead. The remaining 5 are alive, 1 to 2 years following surgery and at the present time are enjoying a complete remission of symptoms. Of the 9, none developed obstructive urinary complaints.

Group 3. In the 5 cases treated by radical surgery plus castration and estrogen therapy, bilateral orchiectomy was performed because malignancy at the time of surgery was found to have extended beyond the limits of the prostatic capsule, or on later examination of sections from the apex, the base of the bladder and vesicles showed marked involvement in the malignant process.

Of 2 cases with apical capsular involvement, 1 patient died 5 years postoperatively of carcinoma of the large bowel which showed none of the characteristics of the prostatic carcinoma and postmortem examination showed no evidence of a return of his former malignancy. The other patient of this type is alive and apparently well after 5 years.

Of the 3 cases that had extension into the seminal vesicles, 1 patient has an extensive recurrence 4 years postoperatively. His life expectancy is less than one year. The remaining two in this group are alive and still enjoying a complete remission from symptoms 2 and 5 years respectively.

Results in this group tend to support the thesis that extension of malignancy beyond the prostatic capsule does not necessarily contraindicate the employment of radical surgery.

Group 4. The 17 cases in which total prostatectomy alone was used seemed to be cases in which the malignancy was confined well within the limits of the prostate itself; but ten of the seventeen showed extension into the fibrous capsule on microscopic examination.

Of this group, 10 patients are apparently well and without evidence of recurrence 1 to 3 years postoperatively.

Two have local recurrences at the end of 2 and 3 years and are unaffected by recent orchiectomy.

One has a questionable symptomless recurrence in the region of the right seminal vesicle, detected at the end of 3 years and unchanged at the end of 5 years.

One has a recurrence anterior to the rectum which first developed at the end of 7 years and as yet has had no further treatment.

Three are dead: one a hospital death; one, 2 months postoperatively met a violent death; and one died 2 years postoperatively of lobar pneumonia, postmortem examination showing no evidence of a return of malignancy.

Of this group of seventeen, three are dead of causes other than carcinoma, four have recurrences 2, 3, 5, and 7 years postoperatively and the remainder are apparently well 1 to 3 years postoperatively.

While the length of life since operation has been, on the average, short thus far, the fact that in 1 case a local recurrence developed at the end of 7 years again points up the need for a 10-year follow-up period before statistics as such can be of much value.

CARCINOMA OF THE PROSTATE TREATED BY PALLIATIVE MEANS

It is perhaps worthwhile to compare each of the last three groups against a background of 70 cases of more advanced carcinoma treated between 1941 and 1946 in which the treatment of choice was palliative: transurethral prostatic resection, orchiectomy and estrogen therapy. First, as to length of life; second, as to the length of the remission with comfort and freedom from symptoms; and third, as to the recurrence of local obstruction and disturbance to urinary function.

During a 5-year period from 1941 to 1946, 70 cases of advanced carcinoma of the prostate were treated by transurethral prostatic resection, castration, and estrogen therapy. Nine patients lived 1 year or less and may be said to have obtained no remission; twenty-seven, 1 to 3 years; twenty-five, 3 to 5 years; and nine over 5 years, some of them 8, 9, and 10 years.

In percentage figures, 13 per cent less than 1 year; 39 per cent 1 to 3 years and 35 per cent 3 to 5 years and 13 per cent 5 years or more.

Obstructive symptoms required a second transurethral resection in 1 case, or 11 per cent, of the first group; in 4 cases, or 15 per cent, of the second group; 6 cases, or 24 per cent, of the third group; and in 4 cases, or 45 per cent, of the fourth group.

Strictures of the prostatic urethra required repeated urethral dilatations in four of the 9 cases of the first group, or 47 per cent; in five of the 27 cases of the second group, or 19 per cent; nine of twenty-five of the third group, or 23 per cent; and eight of the 9 cases in the fourth group, or 88 per cent.

In other words, the longer the remission the higher the percentage that developed obstructive symptoms which required further transurethral resection or dilatation.

While these patients receiving palliative treatment were more advanced ones at the time treatment was instituted, the reappearance of obstructive symptoms is evident and apparently in direct proportion to the length of life. In contrast to this, none of those treated by perineal surgery have as yet developed such complications.

Of perineal groups 2 and 3, which are essentially palliative procedures, six are dead, three of them of prostatic carcinoma, 1 to 2 years following surgery. Eight are alive from 1 to 5 years with evidence of recurrences but without obstructive symptoms, and one is apparently well 5 years postoperatively.

Of perineal group 4, in which the malignancy was confined to the prostate itself at the time of surgery, three are dead from causes other than prostatic malignancy, fourteen are alive, four with recurrences, 2, 3, 5, and 7 years, respectively, and ten are alive without evidence of recurrences from 1 to 3 years.

CONCLUSIONS

For this series another 5 years will be necessary before comparison of the results of surgical removal with recognized palliative measures will be available. Meanwhile, some encouragement is to be found in the lower mortality rate from prostatic carcinoma in the cases in which surgical removal has been employed, and the longer period of remission with the absence of local obstructive recurrences in those cases in which cure has not been obtained following radical removal combined with palliative therapy.

All of us could wish that the figures on the results of perineal surgery were more impressive and optimistic. But until research discoveries offer us something surer than total surgical removal, we should employ our available procedures to the utmost.

Our great need in the future is for the institution of a definite program of early detection sponsored by the American Urological Association, its Sections and other organizations interested in and equipped to stress this need to the public and to our own profession; for a program to stimulate the interest of urologists in this problem and one equipping them with the necessary training and ability to do the indicated surgery, for it is surprising how such cases appear in one's practice once it is known the individual can and will detect and remove malignancy if in the operable stage.

So let each of us return to his practice determined to meet this challenge, determined to develop his ability to the utmost. For there is no place for defeatism in as young and vigorous a specialty as urology.

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THE TREATMENT OF LATE RELAPSE IN PROSTATIC CARCINOMA BY CORTISONE

W GIFFORD HAYWARD

Following the monumental work of Huggins which he reported in 1941, untold numbers of men, the victims of prostatic carcinoma, have had a prolongation of life and have had their last days made easier with hormone therapy, and of course castration is a big part of hormone therapy

Huggins[1] states that "androgens cause both normal and neoplastic prostatic tissue to grow and secrete The urinary 17-ketosteroids average about the same level in prostatic cancer as in other men of that age but enough androgen is produced to make a tumor grow vigorously if untreated In certain cases following orchiectomy the adrenal continues to produce androgens which can be controlled to some extent by estrogens In other cases death ensues with the primary tumor greatly inhibited but metastatic areas grow vigorously and in still others the growth is too primitive to be influenced by hormones It is now known definitely that the adrenal is the sole agency producing androgen in castrated men"

Frame and Jewett[2] state "that there is abundant evidence to indicate that the testis is not the sole source of the urinary 17-ketosteroid and that the adrenal cortex is the one, if not the only extra testicular source, that the testes do not contribute to the 17-ketosteroid output in the older age group or the removal of the testes results in an increased contribution by the adrenal cortex Estrogenic substances while combating the effect of this androgenic hormone still stimulate its production in the adrenal through the luteinizing hormone of the pituitary The time then arises, if the patient has not already succumbed to some intercurrent disease, that a relapse occurs and from that time on there is a rapid decline"

Recent reports have appeared in the literature of bilateral adrenalectomy and still later hypophysectomy followed promptly by great improvement in these carcinomatous patients who were on the decline Although of experimental interest, these operations seem too radical to be adopted by the average urologist These few reports formed the background of my awakened interest in hormonal therapy and the opinions that I have formed are the subject of the following discussion Briefly I should like to review with you the physiology of the endocrine glands that are pertinent to the subject of prostatic carcinoma, namely, the testes, pituitary and adrenals We must accept from work that has been done before that the anterior pituitary is the only regulating center of most of the endocrine glands It exerts its influence on the other glands by means of trophic hormones In response to this, these target glands produce tissue affecting hormones (Reifenstein)[3]

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[1] Huggins, C and Scott, W W Ann Surg, **122:** 1031-1041, 1945

[2] Frame, E and Jewett, H J J Urol, **52:** 330-333, 1944

[3] Reifenstein, E C Pathologic Physiology, Wm A Sodeman, Philadelphia W B Saunders Co, pp 513-555

The anterior pituitary contains three types of cells; acidophilic, basophilic and chromophobe. Only the first two interest us. The acidophilic cells produce the growth hormone, the thyrotrophic hormone, adrenocorticotrophic (ACTH) and perhaps gonadotrophic hormone.

The basophilic cells are all gonadotrophic:

a. Follicle stimulating hormone.

b. Luteinizing hormone.

c. Luteotrophic hormone (but this is a hypothetical hormone which is supposed to maintain the corpus luteum. It is identical with the gonadotrophic hormone previously mentioned but may be produced by the acidophilic cells). Of the hormones produced by the acidophilic cells the adrenocorticotrophic hormone is the one that interests us in this discussion. This stimulates the adrenal cortex to produce the sugar hormone or (S) hormone. The adrenal cortex produces desoxycorticosterone and an androgenic hormone.

Present investigation has not definitely determined whether ACTH has stimulated their production, whether they are due to stimulation by other or luteinizing hormones or whether their production is independent of pituitary control. The trophic hormones of the basophilic group are qualitatively identical in both sexes. Both the follicle stimulating hormone and the luteinizing hormone are of interest to us because in the female the former stimulates the production of estrogen and in the male the production of spermatozoa. In the male the luteinizing hormone stimulates the Leydig cells to produce androgenic hormone. There is fairly convincing evidence that the luteinizing hormone or the luteotrophic hormone stimulates the adrenal cortex to produce in both sexes an androgenic hormone similar to the androgen produced by the testes which has protein anabolic properties and which leads to the excretion of 17-ketosteroids in the urine.

It is apparently axiomatic that there is a governing control over the production of hormones. For example, after the luteinizing hormone of the pituitary has stimulated Leydig cells to produce androgenic hormone and a sufficient quantity has been produced, the Leydig cells in some way retard further action by the pituitary to prevent over production. Now, if the testicles are removed by castration, not only is the testicular source of androgen removed but also the retarding power is removed.

Hotchkiss[4] states "that the pituitary gland of castrated animals exercises a greater stimulation of the sex glands when implanted into normal animals thereby suggesting that the pituitary activates and is restrained by the sex gland hormones."

Greep and Jones[5] state "that the pituitary of the castrate has a rich content of gonadotropine and an increased output of these hormones. The adrenal gland may in turn form a retarding substance to prevent overstimulation but the fact remains that the adrenal is producing androgenic hormones that are the bane of prostatic carcinoma."

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[4] Hotchkiss, R. S.: Fertility in Men. Philadelphia: Lippincott, 1944.

[5] Greep, R. O. and Jones, I. C.: Symposium on Steroid Hormones, E. S. Gordon: Madison: University of Wisconsin Press, p. 551.

The object in view then is to minimize or abolish the adrenal production of androgenic hormone. Reifenstein in his reference to Selye's adaptation syndrome makes the statement that recent evidence suggests that the sugar hormone (cortisone) inhibits the production of nitrogen hormone or androgenic hormone. It has also been shown by Wilkins and his associates[6] and by Bartter and his colleagues[7] that the elevated 17-ketosteroid excretion in the adrenogenital syndrome can be reduced practically to zero by the administration of cortisone. And again it has been shown that the continuous administration of an excess of any hormone (trophic or tissue affecting) may result in atrophy of the gland that is the endogenous source of the hormone.

Sprague et al.[8] have made the following points:

1. Cortisone causes a depression of the endogenous production of adrenal cortical hormone.
2. Experimentally, cortisone causes atrophy of adrenal cortices in rats.
3. A depression of urinary 17-ketosteroids occurs during and subsequent to administration of cortisone.
4. In general, the effects of cortisone or adrenal cortical structure and function are the opposite of those of pituitary adrenocorticotrophic hormone.

Greep and Jones are of the opinion that "histologically and functionally the adrenal cortex is divided into three zones, the outer zona glomerulosa, middle zona fasciculata and the inner zona reticularis. Experimental work on rats tends to show that the outer zone produces desoxycorticosterone independent of pituitary influence, the middle zone produces the S hormone dependent on pituitary stimulation and the inner zone produces androgenic hormones dependent on the pituitary. There has been little experimental opportunity to study the adrenal histologically in the human but they report one woman who had marked pituitary atrophy, with normal zona glomerulosa of the adrenal and atrophic zona fasciculata."

Cortisone or the sugar hormone is produced by the adrenal following stimulation by ACTH. Although urine of children under eight contains corticosteroids there is no 17-ketosteroid. Yet, stimulation with androgens before that age will cause 17-ketosteroids to appear. It is therefore improbable that the pituitary does stimulate the adrenal cortex with this hormone before that age. This is the basis for the belief that the pituitary produces two kinds of ACTH, one for the sugar hormone and the other for the N hormone or androgenic hormone. It would seem unwise then in prostatic carcinoma to try to obtain the cortisone action by using ACTH. Rather, cortisone should be used for its replacement effect to produce partial adrenal atrophy.

Now in addition to this all important effect, cortisone has side effects which are in the main, beneficial. There is an increase in appetite which in turn causes a gain in weight. Its effect is euphoristic and increases mental capacity and activity. Although cortisone causes some fluid retention, its effect on electrolytes is only about 3 per cent of the desoxycorticosterone effect. Patients taking it should have

[6] Wilkins, Lawson, et al.: J. Clin. Endocrinol. and Metab., **12:** 3, 1952.

[7] Barrter, F. C. et al: Pathologic Physiology, Wm. A. Sodeman; page 551.

[8] Sprague, R. G., Power, M. H., and Mason, H. L.: Physiological effects of cortisone and pituitary adrenocotrophic hormone (ACTH) in man. J.A.M.A., **144:** 1341–1347, 1950.

a restricted sodium intake. Even then they may have to be given diuretics occasionally. If there is too much loss of potassium as evidenced by loss of energy and muscular weakness it may be detected by electrocardiographic changes and potassium then administered to make up the loss. Its contra-indications are: 1) congestive heart failure, 2) psychotic tendencies, 3) tuberculosis, 4) active ulcer, 5) diabetes and 6) renal insufficiency.

During treatment it is well to do a weekly urinalysis; blood sugar determination if the patient is glycosuric and a glucose tolerance if the patient is hyperglycemic.

CASE REPORT

W. S. B. aged 81 was referred to me in 1942 because of slight dysuria. A preoperative diagnosis of carcinoma of the prostate was made and an endoscopic resection was done. Bilateral orchiectomy immediately followed and stilbestrol was faithfully taken. His progress was satisfactory until the summer of 1951, when he again had dysuria. Rectal examination showed no induration and very little prostate but cystoscopic examination showed carcinomatous tissue in the prostatic urethra which was again resected. His decline became very rapid characterized by loss of weight and strength and severe perineal pain. This became so severe that it was necessary to institute around the clock nursing and the administration of narcotics both orally and by hypodermic every few hours. The patient was an intelligent man and knew the reason for his pain and asked only that his last days be made as comfortable as possible.

At about this time the reports of bilateral adrenalectomy came to my attention, and although I knew the patient was in no condition to undergo such a radical procedure, the thought occurred to me that some atrophy of the adrenals might be obtained by using replacement therapy. This was talked over at great length with the patient and he consented to give it a trial. Treatment began in September 1951, with 100 mg. of cortisone a day reducing it rapidly to 25 mg. per day. For the first 6 days practically no change was evidenced. Then almost, immediately the results became dramatic. Appetite and strength returned amazingly, and although metapon was continued it became apparent that other narcotics by hypodermic could be abandoned. Instead of resigning himself to die he made plans to move to his winter home in Florida, which he did. The following excerpt from a letter was received December 11, 1951: "Reporting for myself, as you suggested, I fully understand that you are dealing in terms of relief and comfort, and not of cure. Nevertheless I have been able to move down here without a jolt and that of itself was impossible until you began the present treatment. But more than that, my increased vigor and strength seem an amazing change. Whereas a few turns about the room was formerly all I was good for, I now walk around town without tiring and spend hours tinkering in my shop. I still have some pain at times, but nothing to compare with the rough going of last summer." Since that time, his nurse has reported at weekly intervals. He arranged and conducted a town meeting in Florida; worked in his shop every day and was able to drive his car where ever he wished to go. It was necessary on two occasions to administer diuretics.

The patient is still comfortable, active and happy (November 6, 1952).

DISCUSSION

Although the value of reporting the results of 1 case may be open to question, the complete absence of mention of this type of therapy in the literature to date and the excellent results, though temporary, make it seem not presumptuous and not premature. Its trial in a large number of cases will determine its value or futility.

ADDENDUM

Since the paper was prepared, two other personal cases and one other case treated by a colleague have all responded favorably to this treatment, J. E., aged 62, had an anaplastic growth. He is now in relapse. No benefit was derived from cortisone therapy (November 6, 1952).

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METASTASIS TO THE CORPORA CAVERNOSA FROM CARCINOMA OF THE PROSTATE

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Involvement of the corpora cavernosa by cancer of the prostate is exceedingly rare. Craig, reviewing the literature in 1941, found only seven examples of carcinoma of the cavernous bodies, either metastatic or by direct extension from a carcinoma of the prostate. He mentioned the patients of Tuffier 1885, Nogues 1929, Guibal and Parie 1929, Paglieri and Schiappapietra 1928, Young 1926, and Cecil 1936. Cecil had seen 2 cases. Young was of the opinion that his case represented a direct extension. Paglieri and Schiappapietra established the histologic diagnosis by aspiration biopsy. Guibal and Parie treated their patient by radium and x-ray, followed by emasculation. All the other patients were surviving only a short time after the diagnosis was established.

Wattenberg in 1944 reviewed the literature on unusual tumors and secondary carcinomas of the penis. He found 19 cases of secondary carcinoma in the penis and added one of his own. Four of those listed gave the prostate as the primary site. He cited Paglieri 1928, Guibal 1929, Martin-Larval 1931, and Peters-Huntress 1938.

The only 2 case reports which we found in the American literature are the following: Frontz and Alyea in 1928 observed a 51-year-old man with priapism of 4 months' duration. Following an incision into the hard cylindrical corpora, gangrene developed and several days following amputation of the penis the patient died of terminal pneumonia. Microscopic examination showed an alveolar malignant tumor in the cavernous bodies. There was a cancerous growth in the prostate composed of spindle shaped cells with vesicular nuclei. Extensive metastases were found at autopsy in lymph nodes and visceral organs, including the lungs.

The second case from this country was reported by Peters and Huntress (1938) in a 64-year-old man who had an inoperable carcinoma of the prostate. From tissue removed by transurethral resection, a diagnosis was made of carcinoma of the prostate. Two weeks later a nodule appeared in the corona of the glans. Other nodules developed in the glans, in both corpora cavernosa and in the spongiosum. Constant priapism was present and a biopsy of the nodules at the corona revealed a metastatic adenocarcinoma. Six months later complete retention occurred due to invasion of the urethra. The chest film showed evidence of metastases in the hilus. Following a suprapubic cystotomy the patient died of acute pulmonary edema.

In view of the rarity of this condition and because of the fact that in the previously reported cases, no patient survived more than a few days after operation, our following observation is reported.

Read at annual meeting, South Central Section, American Urological Association, Houston, Texas, October 31, 1951.

CASE REPORT

Mr. W. C., a white man 79 years old, was admitted on October 11, 1950 with the complaints of persistent painful erection of the penis and inability to void. His illness had begun rather insidiously about a year prior to admission, at which time he noticed nocturia of 5 to 6 times a night and frequency of every hour to half-hour during the daytime. He also noticed slowness of stream. These symptoms became progressively worse until the time of admission when he suffered complete urinary retention. In January 1950, he first noticed that his penis was becoming firm and painful. This condition gradually became worse until the penis maintained a condition of erection at all times. About three months prior to admission the patient noticed a small pea-sized nodule on the glans penis. This was removed by another physician who made a diagnosis of carcinoma of the penis.

The patient had never had gross hematuria. He had never passed a stone. He had always been in good health up to the onset of the present illness. His only operation had been a hemorrhoidectomy in 1949, following which he suffered an inflammatory stricture of the rectum. He had never had a serious injury.

Physical examination on admission revealed an alert and cooperative patient of the stated age. The temperature was 99F, respiration 18 per minute, pulse 76, and blood pressure 150/70. The weight was 140 pounds. His average weight for the past several years had been 160 pounds. The heart was slightly enlarged and there was a loud systolic murmur audible at the apex of the heart. The chest was normal and there were no abnormal findings in the abdomen. There was no inguinal adenopathy. Reflexes were normal and there was good co-ordination. The penis was erect and was in a state of persistent priapism. It was stony hard to palpation. There was a nodular area on the glans which was about the size of a pea; however, there was no break in the mucous membrane at any point and no ulceration. Rectal examination showed the rectum to be spastic due to an inflammatory stricture of the rectum. This made it difficult to examine the prostate with any degree of accuracy, although the prostate felt hard.

Laboratory examination on October 11, 1950 revealed erythrocytes to be 3,290,000, hemoglobin 65 per cent, leukocytes 8,350 with 64 neutrophiles, 2 band forms, 1 eosinophile, 28 lymphocytes, and 5 monocytes. Urine was acid in reaction, had a specific gravity of 1.011, no albumin or sugar, and it contained 3 or 4 pus cells per high power field. Kline and Wassermann tests were negative. Acid phosphatase was 3.5 and alkaline phosphatase was 7. The nonprotein-nitrogen was 34 mg., the creatinine was 1.65 mg. Sedimentation rate showed a total of 32 in one hour. Urine culture showed the presence of B. coli.

X-rays of the chest showed increased bronchial markings but no evidence of metastases. A plain urogram showed the kidneys to be of normal size and position. The osseous structures showed hypertrophic changes from the margins of the lumbar vertebrae. There was no evidence of urinary or biliary calculi. Psoas shadows were distinct. There was no evidence of metastasis to the bone of the pelvis or spine.

During the next few days the patient was kept on catheter drainage and the bladder was gradually decompressed until empty. Whole transfusions of blood were given October 12 and 13, and intravenous fluids were given as indicated.

On October 24 a biopsy of the nodule on the glans penis was made. Pathologic report: The biopsy specimen from the glans penis consisted of three small pieces, from 3 to 4 mm. in diameter. They were grayish-red in color and their consistency was firm. The microscopic structure was greatly distorted due to cautery effect. In the largest piece part of the specimen showed an invasive tumor growth. It was composed of large sheets of polygonal and oval cells with dark nuclei. No horn pearls and no intercellular spines could be recognized. There were no glandular structures. Histologic diagnosis: Solid carcinoma of glans penis.

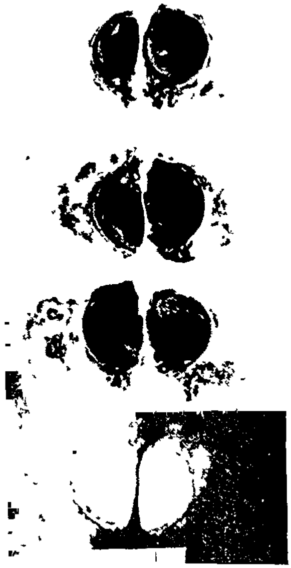

FIG. 1. Coronal section through cavernous bodies. Septum invaded except in uppermost (proximal) portion.

On October 31, 1950, a radical amputation of the penis was done, following which the urethra was transplanted to the perineum. In spite of his age the patient withstood the operation satisfactorily and made good and rapid recovery.

Pathologic report: The penis was extirpated with the cavernous bodies intact. The length of the entire specimen was 14 cm. and the greatest width was 4 cm. Normal appearing skin covered the distal half of the penis. The deep fascia surrounding the cavernous bodies appeared normal. The shaft and glans were extremely firm, in a state of erection. Multiple coronal sections showed both corpora cavernosa transformed into cylindrical masses of solid tumor. The cut surface of the corpora was grayish-white and compact. Few blood-filled spaces were recognized in the proximal half of the penis. The septum between the cavernous bodies was intact in the proximal third of the specimen but invaded by tumor tissue in the anterior portion. The deep fascia covering the corpora was not invaded. There was extension of the tumor to the left side of the glans and an area representing the site of biopsy was noted near the corona. Beneath the corpora cavernosa, the 7 cm. long urethra had a normal lumen and the corpus spongiosum was soft and free of tumor tissue. No tumor thrombi could be recognized in the deep dorsal vein or its branches.

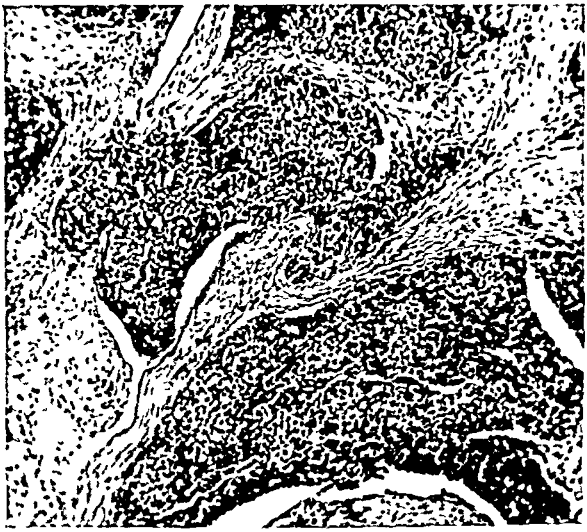

FIG. 2. Blood sinuses of corpus cavernosum invaded by tumor strands

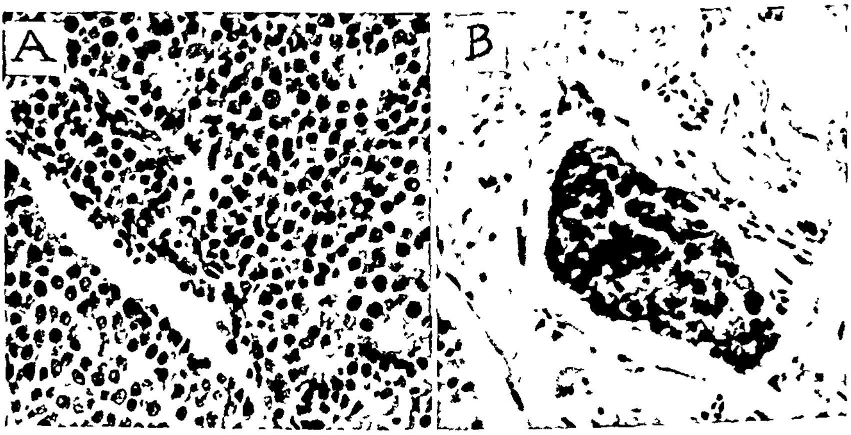

FIG. 3. *A*, tumor in corpus cavernosum. Solid and indistinct glandular structures. *B*, single group of cancer cells in cavernous space.

Microscopic study of multiple sections through the corpora cavernosa revealed sheets of tumor cells occupying almost all blood sinuses. Most cavernous spaces were completely filled out with tumor cells and many had an intact endothelial lining. There was in several areas destruction of the trabeculae, with confluence of large cavities filled with tumor cells. The tumor cells were arranged in solid masses, without fibrous stroma; most sheets of cells were compact, however in some sections more or less distinct small spaces surrounded with tumor cells were recognized. The cells were polygonal or oval, and low cuboid when arranged around the lumens. Their nuclei were dark stained, varied in size and form. Few mitotic figures were seen. While the septum was invaded by tumor cells in the distal portion of the penis, the deep fascia was intact. Histologic diagnosis: Metastatic solid carcinoma of both corpora cavernosa and of the glans penis.

The microscopic sections were studied by Dr. A. C. Broders who made the following diagnosis: Grade 3 adenocarcinoma, probably metastasis from carcinoma of the prostate or from the gland near the neck of the bladder. Dr. Fred W. Stewart of Memorial Hospital in New York concurred in the diagnosis of metastatic carcinoma.

On November 14 a transurethral resection of the prostate was done through the transplanted urethra.

Pathologic report: The specimen consisted of many slender pieces of prostatic tissue. Their length varied between 4 and 12 mm. and the width between 4 and 6 mm. Many pieces were soft and of yellowish-brown color. There were several pieces which had a whitish color and a much harder consistency than the others. Eight brown, hard concretions, between 1 and 2 mm. were also removed.

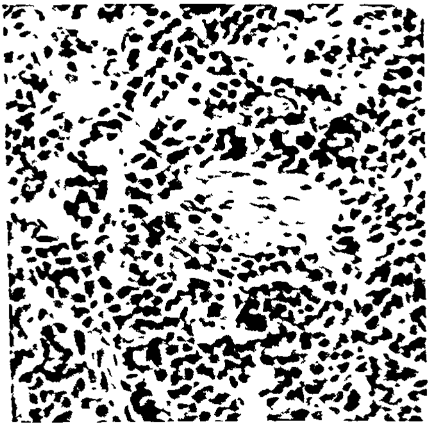

FIG. 4. Primary prostatic carcinoma. Solid strands of undifferentiated adenocarcinoma.

Microscopic examination: Microscopic examination of the prostatic tissue revealed an invasive growth in fibrous stroma. There were narrow strands and wider columns composed of atypical cells with dark oval nuclei and light oxyphilic cytoplasm. Marked variation in size of the nuclei was noted. There were no distinct glandular lumens. Histologic diagnosis: Undifferentiated adenocarcinoma of the prostate.

Recovery from the resection was uneventful and the patient was dismissed from the hospital on November 29, 1950. At that time he was up and about and voiding a good free stream. He has been followed up in the office and sounds have been passed at regular intervals. Chest films and plain urograms have remained negative for spread of tumor. At present, 1 year after operation, no evidence of local recurrence in the perineum or of metastases to other organs can be found. His only complaint at present is that the end of his penis still pains him 1 year after removal of the penis.

DISCUSSION

Metastatic prostatic carcinoma in the corpora cavernosa has been regarded until recently as a terminal and hopeless condition. In almost all cases in the literature death followed shortly after operation. We placed our patient on estrogen therapy after operation. Since the introduction of hormonal therapy, which has changed the prognosis of cancer of the prostate profoundly, metastatic carcinoma of the penis must be regarded from a less pessimistic view. For our case we cannot accept the standpoint of Young that involvement of the cavernous bodies is to be explained by direct extension from the prostate. First, we were unable, after extirpation of the penis, to demonstrate a tumor growth continuous from the prostate to the corpora cavernosa. Second, the fact that the firm tumor nodule appeared on the glans penis does not favor the view that the cavernous bodies were invaded by direct extension from the prostate. We believe that our case represents a true metastatic lesion, probably through the deep dorsal vein of the penis. Batson demonstrated connections between the prostatic plexus of veins and the deep dorsal vein. By increasing intrathoracic and intra-abdominal pressure (coughing or straining) blood may be squeezed out from the pelvic veins into peripheral veins. In this way tumor fragments present in prostatic veins may be transported retrograde to the cavernous bodies, if the valves of the dorsal vein are defective. We were unable to detect any metastasis in other parts of the body, especially in the lungs, which makes the idea of arterial emboli as cause of metastasis unlikely in our case.

The fact that our patient is alive and does not show evidence of perineal recurrence or distant metastases makes extirpation of the penis seem justifiable to us and more than a palliative procedure. Since hormonal therapy will not, however, lead to complete cure of prostatic cancer, we may never expect to obtain the results as reported recently by Cattell and Mace. Their patient was alive and well 9 years following excision of a penile metastasis and 11 years after resection of a primary rectal carcinoma. In their case, the lesion in the cavernous bodies was apparently the only metastasis.

SUMMARY

A case of cancer of the corpora cavernosa secondary to carcinoma of the prostate is reported. This brings the total number of cases in the American literature to three.

Priapism was the presenting symptom of the penile lesion in our case, as in most of the others reported. Most patients with metastatic prostatic carcinoma in the cavernous bodies died shortly after operation. Our case, the first observation since hormonal cancer therapy has been introduced, lets this condition appear less hopeless, especially if the penile tumor is the only metastatic lesion, as we believe it was in our case. Our patient is alive and well 1 year after extirpation of the penile growth He enjoyed his eightieth birthday party very much.

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GIANT CONDYLOMATA ACUMINATA (CARCINOMA-LIKE CONDYLOMATA OR BUSCHKE-LOEWENSTEIN TUMORS) OF THE PENIS

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Condylomata acuminata are a variety of warts which have a predilection for moist mucocutaneous surfaces. Numerous theories as to their origin have been proposed, and simple to fantastic methods have been used to treat all types of warts. They are auto-inoculable and transmissible, and are probably caused by a filtrable virus. The role of the prepuce and irritating preputial secretions in the development of condylomata has been stressed by Gersh.

Simple condylomata acuminata of the penis are benign, highly vascular, friable, noninvasive papillary growths. Their most frequent site is within the confines of the preputial cavity.

In contrast with these relatively small excrescences there are a rare variety of large warty growths of the penis known as giant condylomata, carcinoma-like condylomata, or Buschke-Loewenstein tumors, which clinically appear to be malignant but histologically are benign and show the same regular orderly arrangement of cells as do simple condylomata acuminata; in fact, microscopic sections show practically identical pictures. The giant condylomata present a clinical picture of malignancy by their luxuriant growth, large size, ulceration, infection, extension, and penetration into the deeper tissues. They grow downward as well as superficially while ordinary condylomata proliferate only above the surface. Simple condylomata of the penis are often malodorous but the giant warts have a particularly foul and pungent odor. The latter growths appear to be infiltrating, but careful examination reveals that they only displace and compress the normal tissues. Loewenstein explained that the invasive characteristic led to the term "carcinoma-like" condylomata. He aptly stated, "We believe, however, that this infiltration is not an active one; that we are dealing here with condyloma tissue which has simply been *displaced* downward by the prolific growth of condyloma above it. The effect of this process is to compress a portion of the corpus cavernosum. Nowhere are tumor cells to be seen; neither in the tissue spaces, blood vessels nor in the lymphatics."

Two cases were described by Buschke in 1896. Buschke and Loewenstein reported 3 cases in 1925 and added another in 1932. Loewenstein in 1939 reviewed the literature and described a patient in whom extensive involvement and destruction of the penis required amputation. However, he recommended conservative surgical treatment with curettage and electrocoagulation when clinically possible and so long as the lesions are not carcinomatous. He found radiation therapy unsatisfactory: this was also the experience of Frei who reported 5 cases and described the development of the lesions. According to him, the growths have their origin in a phimotic preputial cavity where they proliferate, later break through

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the skin surface in the region of the dorsal lymph vessels and form a circle of protruding condylomatous masses. The glans penis finally becomes exposed and the prepuce hangs down as an empty sac. Condylomatous masses may eventually completely cover the penis. Frei recommended biopsy of the lesions followed by conservative surgery, and amputation of the penis only in cases of repeated recurrences. He stated that the condition was known to earlier venereologists, who considered it a form of syphilis. He also referred to an atlas by Picord published in 1851 in which attention was directed to the similarity of this disease and carcinoma.

Muhlpfordt in 1928 shared the opinion of other workers at that time, most of whom considered these lesions potentially malignant and treated them accordingly. He described the case of a 19-year-old boy treated by amputation with no recurrence. In 1931 he reported a giant condylomatoid tumor of the penis in a 52-year-old man in which early carcinoma was found. Herman described the case of a 40-year-old patient with extensive condylomata of the penis in which a mass of papillary carcinoma perforated through a slough in the prepuce. Treatment with radical amputation and radiation was followed by rapid recurrence and death.

Treite discussed pointed condylomata of the external genitalia in women and presented a patient with multiple recurrences over a twelve-year period followed by development of squamous cell carcinoma. He raised the question as to whether pointed condylomata should be regarded as precancerous affections, but emphasized the fact that in only occasional instances are these growths the basis of malignancy. He suggested repeated biopsies in cases which persist or recur, so that if malignancy is present it may be detected.

CASE REPORTS

Case 1. E. G., a 39-year-old, married, white truck driver, was admitted to Colorado General Hospital on June 21, 1944 with papillomatous ulcerative lesions on the penis. For this condition he had six admissions with a total hospital stay of 298 days when finally discharged on May 23, 1951.

In 1937, he first noted a wartlike lesion under the prepuce. Several more growths developed later, slowly increased in size, and eventually perforated through the dorsum of the prepuce. The patient denied having had any extramarital exposure or venereal disease.

Physical examination, at his first admission in 1944, revealed no definite abnormalities except for the penis which was swollen and involved by three fungating ulcerative masses, each about 3 cm. in diameter, projecting from the dorsum of the prepuce and penile shaft. A foul-smelling purulent discharge exuded from the lesions. Laboratory studies showed normal urinary findings. There was moderate leukocytosis. Serological tests for syphilis were negative. Sedimentation rate was slightly elevated. Blood nonprotein nitrogen and sugar were within normal limits. Frei test was negative. Cultures of the exudate grew Staphylococcus aureus; no molds were identified. Biopsy of the lesions was reported as "cutaneous papilloma." Treatment consisted of potassium iodide orally, hot compresses of boric acid solution, and a course of deep x-ray therapy. The patient was discharged September 15, 1944.

On October 5, 1944, he was readmitted and started on injections of a vaccine prepared from autolysate material. Five days later he was discharged from the hospital with instructions to continue the vaccine injections at his local physician's office; he failed to do this. On July 12, 1946 he was again admitted to the hospital; the growths had proliferated considerably. I first saw the patient at this time (fig. 1, *A*). Clinical laboratory and histologic studies were repeated without finding a specific cause for the lesions. On July 20, 1946 an operation was performed in which the swollen distorted prepuce and many penile lesions were resected. On July 29, 1946 most of the remaining lesions were curetted out and resected; in some areas the dissection extended to Buck's fascia. Deep growths in one portion of the glans were not completely removed because of severe bleeding. Following this procedure a urethral fistula developed. The dermatology department was considering the possibility of the lesions being granuloma inguinale and administered a course of tartar emetic intravenously. On September 6, 1946, the resected areas were clean and healing; it was planned to remove the remaining lesions if the tartar emetic did not resolve them, but on this day the patient left the hospital against medical advice.

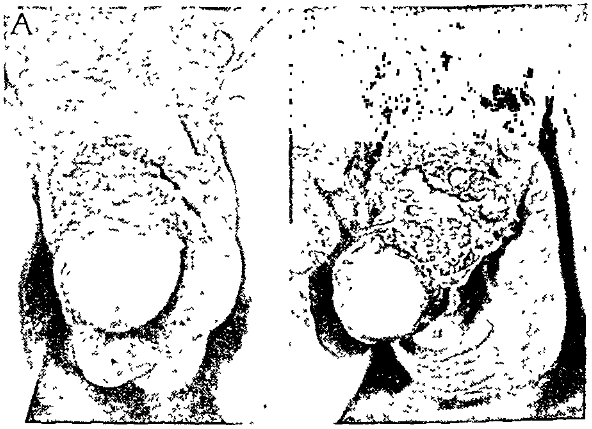

FIG. 1. Case 1. *A*, penile lesions in July 1946. Much of prepuce has sloughed; remainder is swollen and distorted. *B*, penile lesions in July 1947.

He was again admitted to the hospital on July 14, 1947. The penile masses were larger and involved a greater area (fig. 1, *B*). Tissue smears for Donovan bodies were negative, but showed E. coli, hemolytic streptococci and diphtheroids. On August 7, 21, and 28 the condylomata were curetted and resected in stages. Some growths were removed from the substance of the corpora cavernosa and from within the glans penis. We believed that the condylomata were finally all excised. The specimens were subjected to careful study; no Donovan bodies were found. A skin graft from the right thigh was made to the healing penile surface on September 25, 1947. The patient was discharged improved on October 6, 1947, with orders to return to the outpatient clinic for follow-up. He was not seen again until

March 12, 1949 when he was readmitted to the hospital with the shaft of the penis involved by larger fungating masses. At this time 20 gm. streptomycin were given during a ten-day period and again the patient was requested to return for follow-up, but failed to do so.

He was readmitted to the hospital on April 3, 1951 with the same complaints as on the previous admission. He was now a chronic alcoholic. Physical examination revealed a well-developed, well-nourished 46-year-old white man. Temperature was 99F; blood pressure 104/70. His breath had a heavy odor of alcohol. Poor oral hygiene and dental caries were noted. The heart and lungs were normal. The liver edge was palpable one fingerbreadth below the costal margin. The entire penis except for a portion of the glans was involved by large, foul-smelling, fungating ulcerating masses from which a purulent exudate oozed with gentle pressure. The immediately adjacent pubic area and scrotum were also covered by the lesions. Potassium permanganate soaks were applied and the patient received aureomycin and penicillin. Biopsies on April 10, 1951 were reported as condylomata acuminata. Donovan bodies were again searched for and not found.

On April 23, 1951, an incision was made in the median raphe of the perineum; the urethra was sectioned, and the proximal portion transplanted into the perineum. This was followed by block excision of the penis and involved adjacent pubic and scrotal areas. Condylomatous masses bathed by exudate were found in the base of the removed penis (fig. 2). Careful search revealed no remaining condylomata. The wound was closed around ample rubber tissue drains. A slough of one angle of the scrotal flap, with considerable purulent drainage occurred several days later. The wound was alternately irrigated with chlorophyll and Dakin's solutions. Secondary closure of the defect was performed on May 14, 1951 and 1 week later the patient was discharged from the hospital with the wound healed except for one small defect which was filling in with clean granulations.

Since his discharge from the hospital I have seen this patient twice, the last time being on August 23, 1951. The wound was well healed; there has been no recurrence of the lesions to this time and the urethral meatus easily admits a 26F sound.

Pathologic findings (abstracted from a detailed report by Dr. H. M. McCormick and Dr. E. K. Rutledge): The surgical specimen, 10 by 9.5 by 3 cm. in size, consists of a resected penis with attached base of pubic skin and subcutaneous tissue. Almost the entire penis is covered by papillary projections and nodules that vary from 1 to 10 mm. in diameter. A lesion on the pubic skin measures 1.5 by 0.3 cm. In sections made transversely and longitudinally along the shaft, the papillary growths appear to be confined mainly to the surface. A mass of growths projecting from the resected penile base 5 cm. deep to the pubic skin surface displaces the normal structures. Microscopically the involved penile areas are covered by keratinized, acanthotic stratified squamous epithelium thrown into pointed, rounded, and bulbous excrescences. The papillary folds exhibit focal parakeratosis, pronounced hyperplasia of the prickle-cell layer, and an orderly proliferation of the noninvasive swollen basal cells. The supporting loose fibroelastic tissue contains numerous engorged capillaries and a light diffuse and perivascular infiltration of lymphocytes, plasma cells, and neutrocytes. The corpora cavernosa are intact except for areas of localized compression by the encroaching growths. Numerous infoldings of the extremely acanthotic epithelium extend deeply into the corpus spongiosum urethrae, compressing and displacing this structure, and approach the urethra closely at one area (fig. 3). The urethral mucosa and submucosa are infiltrated by neutrocytes, lymphocytes, and plasma cells. Numerous gram-positive cocci and bacilli are scattered within the epidermal debris along the papillary folds basally. No intracellular bacilli or Donovan bodies are detected in Giemsa and Gram-stained sections. As in the previous sections no malignant alterations are detected. Diagnosis: Papilloma, skin, genital region, multiple (condylomata acuminata).

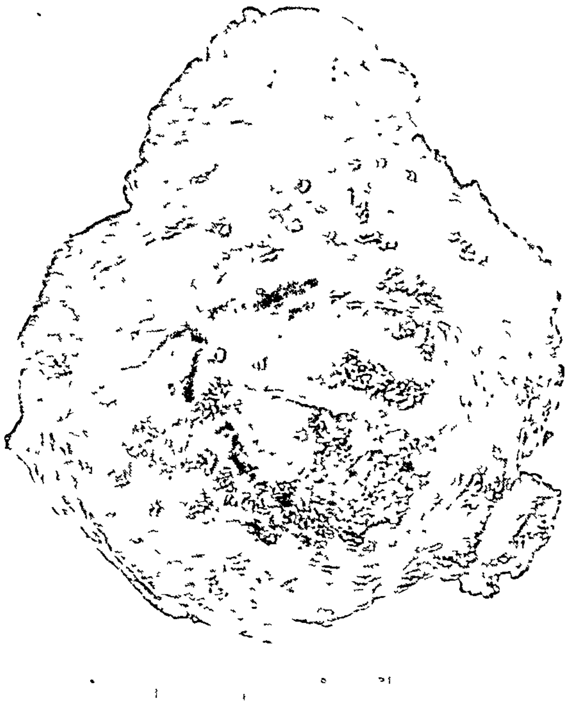

FIG. 2 Case 1. Base of surgical specimen Note condylomata within depths of penile base

Case 2. P. A. B., a 51-year-old white automobile electrician, was admitted to St. Anthony Hospital, January 23, 1950, complaining of penile growths.

In 1934, small warts in the preputial sac were discovered during a pre-employment physical examination. The patient was admitted to a general hospital where an intern made a dorsal slit and "cut off the warts with scissors" under local anesthesia. Marked swelling of the penis developed and persisted for several weeks. One wart had not been removed, and about a year later the patient noted growth of this lesion and the appearance of other warts which eventually ruptured through the dorsum of the prepuce. He treated himself with calomel powder and potassium permanganate soaks. In August 1947, he became acutely ill with fever, and pain in both inguinal regions. His physician attributed the symptoms to the warts and gave the patient a daily injection of 300,000 units of penicillin for 20 days. In March 1948, he was admitted to a private hospital where biopsies were taken. Postoperative hemorrhage required secondary fulguration. Within the next few weeks the condylomatous masses proliferated wildly; the patient was rehospitalized; more warts were resected, and deep x-ray therapy was given followed by a daily penicillin injection for 40 days. Several weeks later his physician again hospitalized him, resected more warts, used mercury bichloride and potassium permanganate soaks, penicillin and streptomycin. Rapid recurrence and proliferation of the warts occurred, and in October 1948, he was hospitalized for treatment with podophyllin ointment. This therapy resulted in more discomfort than the patient would tolerate. In January 1949, he was given aureomycin and took a total of 96 capsules (250 mg. each) during a period of 3 weeks. For several years he had had low grade fever and malaise. Within 2 days after starting aureomycin he noticed improvement in his general well being, the foul odor of the lesions improved, and he became afebrile. However, the warts continued to proliferate and bleeding from the lesions occurred with increasing frequency. He began to carry oxycel and gelfoam gauze so as to control hemorrhages.

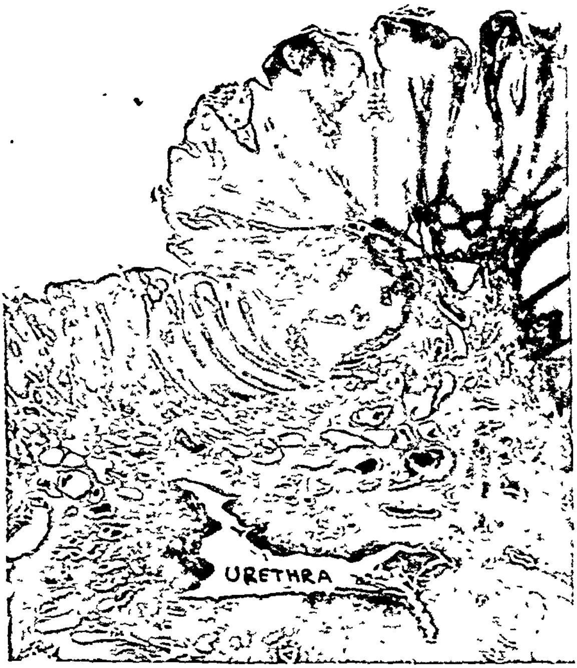

FIG. 3. Case 1 Low power view of section showing compression by condyloma of corpus spongiosum urethra. Note orderly proliferation of epithelium.

He changed physicians and was admitted by Dr. J. B. McCloskey to St. Anthony Hospital on May 26, 1949, for a ten-day period. Under general anesthesia numerous warts were resected electrosurgically. They were reported by the pathologist as "condylomata acuminata from penis and scrotum."

The patient was referred to me while he was in the hospital during this convalescence. The penis was still involved by multiple large warts. On the basis of my experience with case 1, it was my opinion that we were dealing with giant condylomata (Buschke-Loewenstein tumor). I felt that the opportunity for conservative surgical management was past and amputation of the penis was recommended. I did not see the patient again until the day before he was readmitted to St. Anthony Hospital on January 23, 1950. He was now anxious to have the proposed surgery, or any other procedure which might eradicate his disease. Except for symptoms due to the condylomata, he had no complaints in a system review. He had had the usual childhood illnesses. He denied syphilis. At 19 years of age he had gonorrhea which cleared up in a few weeks. Three years later, a few weeks after he was married, balanoposthitis developed which cleared promptly with simple therapy. His wife is healthy and they have three grown children.

Physical examination revealed the following pertinent findings. There were a few small discrete glands in both inguinal regions. The shaft of the penis was practically covered by large malodorous fungating masses; in some areas a purulent discharge was present. The glans penis was the least involved. There was a rosette of condylomata around the base of the penis. The entire penis was indurated and there was at least one urethral fistulous opening just proximal to the glans.

Laboratory data: Numerous diagnostic procedures had been performed during previous hospitalizations. Serologic examinations for syphilis and skin tests with Frei antigen were always negative, as were tissue smears and stains for Donovan bodies. These studies were again made and were reported to be negative. Urinalysis showed no abnormality. Blood count was normal except for mild leukocytosis. Blood serum protein was 7.0 gm. per cent with serum albumin 4.4 gm. and serum globulin 2.6 gm. Sedimentation rate (Wintrobe) was 35 mm. in 1 hour. Stained smears from the warts showed gram-positive cocci and numerous gram negative bacilli, and cultures grew Aerobactor aerogenes, E. coli, and Staphylococcus albus. Chest x-ray showed no pulmonary disease.

Preoperative treatment was directed toward eliminating the secondary infection and consisted of wet packs of zephiran, aureomycin orally, and penicillin intramuscularly. Operation was performed on January 26, 1950 under general anesthesia. A perineal incision was first made; the urethra was sectioned and the proximal portion was transplanted into the perineum. Amputation of the penis was then performed using an incision to include a cuff of healthy surrounding skin (fig. 4, *A*). The patient had an uneventful convalescence, and he was discharged from the hospital on February 9, 1950 with the wounds well healed.

Pathologic report (Dr. A. W. Freshman): "Grossly, the specimen consists of a penis measuring 13 cm. in length and approximately 7 cm. in diameter. The shaft is covered almost entirely by large warty, grey-brown growths, which also extend up on the skin surrounding the base of the penis. There is a cuff of normal skin at the proximal end of the mass. On sectioned surface the urethra is found to be studded with the same type of growth as seen on the surface, and the tumor has invaded the corpora cavernosa and spongiosum. In these regions the tumor is grey-white, rather soft and friable (fig. 4, *B*). The remainder of the tissue is elastic in consistency. Microscopic sections through the urethra, the surface of the penis and the corpora show identical histologic structure of the papillary growths. They are covered by keratin beneath which is stratified squamous epithelium which is markedly thickened. Some of the nuclei are hyperchromatic and chromatin is distributed in the form of dots. Occasional mitotic figures are seen. The nuclei are oval. In the epithelium and in the subepithelial layers are collections of round cells. In the corpora cavernosa are thin walled capillaries, also focal accumulations of plasma cells and lymphocytes. Pathologic diagnosis: Condylomata acuminata of the penis."

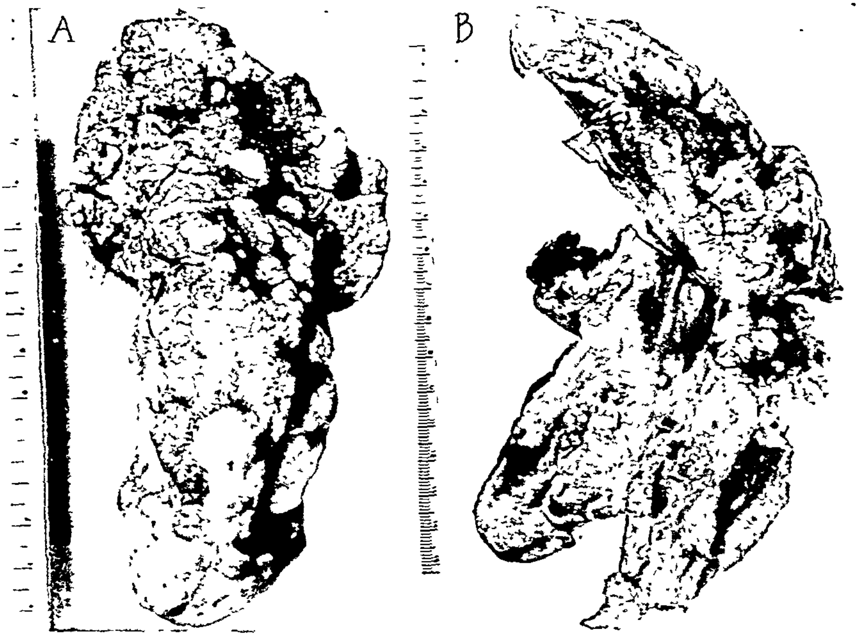

FIG. 4. Case 2. *A*, surgical specimen. Note giant condylomata and distortion of penile surface from repeated resections and fulgurations. *B*, longitudinal section of penis. Condylomatous masses within depths of penis and in substance of corpora.

Since being discharged from the hospital, the patient has been observed at monthly intervals. He is working regularly. There has been no recurrence of the lesions up to the present time.

DISCUSSION

Various modes of treatment for simple condylomata have been advocated by different workers. In a 42- month period in an army station hospital I observed and treated 150 soldiers with simple condylomata acuminata of the penis. It made little difference how the warts were removed; if circumcision was performed concomitantly, thereby ablating the preputial sac and removing the chief nidus for these growths, recurrences were extremely infrequent. However, recurrences were the rule rather than the exception when circumcision was not performed. The necessity for circumcision as part of the treatment for condylomata in the preputial cavity cannot be too strongly emphasized.

Two patients with giant condylomata of the penis are reported. One man had had lesions for 14 years and the other for 16 years. Delinquency of the patients in obtaining medical assistance and failure to apply adequate therapy early, contributed to the development of a condition eventually requiring radical treatment. The lesions at their onset were apparently simple verrucae within the preputial cavity, but later assumed the characteristics of giant condylomata. Complete early removal of the lesions combined with circumcision probably would have eradicated the disease process. The mechanical role of the prepuce in the development and downgrowth of these giant lesions has been stressed by Loewenstein who points out the fact that similar lesions in the female have not been reported.

Even during the patients' last admissions, individual superficial lesions could be curetted out, because there was no cellular infiltration, as in malignancy. The presence of condylomata in the depths of the penile tissues, within the corpora themselves, precluded complete removal of the lesions without excision of the involved structures, and made penile amputations necessary. Further follow-up over a period of several years is planned in both cases.

SUMMARY

Giant condylomata acuminata of the penis (Buschke-Loewenstein tumors) are a rare form of verrucae which begin as apparently simple condylomata in the preputial cavity; they proliferate, invade the normal tissues, displace and compress them. In spite of a clinically malignant appearance—their luxuriant growth, large size, extension, ulceration and infection—the lesions are histologically benign. Conservative but adequate surgical therapy is indicated whenever clinically feasible, but the possibility of carcinoma occurring in condylomatoid tumors must not be overlooked.

Two patients with giant condylomata acuminata of the penis were finally treated by amputation and apparently cured. It would seem that early complete removal of the lesions combined with circumcision would obviate the necessity for such radical procedures.

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AMPUTATION AND RADICAL LYMPH GLAND DISSECTION IN CARCINOMA OF THE PENIS: AN OPERATIVE TECHNIQUE

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Carcinoma of the penis must be treated by early and adequate surgery. If the growth involves only the glans, or the distal one-half of the shaft of the penis, it is the consensus of opinion that amputation 2 cm. proximal to the area of palpable induration will satisfactorily control the primary lesion. Cancer of the body of the penis may remain localized for a long time, but extension finally takes place into the erectile tissue. If the latter has occurred, complete removal of the organ is required. Metastasis occurs earliest and most frequently by way of the lymphatics.

An adequate surgical approach demands not only control of the primary lesion, but also, the complete and careful dissection of the areas of lymphatic drainage. This entails the wide removal of the lymph glands and fat of the femoral and inguinal regions on both sides of the body, as well as the lymph glands along the course of the iliac vessels and at the bifurcation of the aorta.

To carry out an adequate dissection, it is essential that the lymphatic drainage of the penis be kept clearly in mind.

The lymphatic drainage of the penis can be broken down into three main systems:[1] 1) The skin and subcutaneous tissues of the penis, including the prepuce and frenum, drain by way of the dorsal lymphatics to the superficial inguinal and superficial subinguinal lymph glands on either side, and occasionally to the deep subinguinal glands; 2) the glans penis is drained by a small plexus of channels which anastomose at the symphysis pubis and then empty directly into the deep subinguinal and external iliac glands; 3) the penile urethra is drained by channels emptying into the deep subinguinal and the external iliac glands (fig. 1).

The inguinal glands vary from twelve to twenty in number and are situated in the femoral triangle. Those which lie above a horizontal line drawn through the terminal point of the saphenous vein are called the superficial inguinal glands. They form a chain which overlies and parallels the inguinal ligament. The superficial subinguinal glands are located below this horizontal line, extending along either side of the proximal portion of the saphenous vein (fig. 2). The deep subinguinal glands lie below the fascia lata and vary from one to three in number. The most superior gland, that of Cloquet or Rosenmuller, is in the lateral part of the femoral ring, if it is present. The middle gland, when present, is in the

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[1] Gray, Henry: Anatomy of the Human Body. Philadelphia: Lea and Febiger, 1942.

femoral canal, and the inferior gland lies just below the junction of the saphenous and femoral vein.

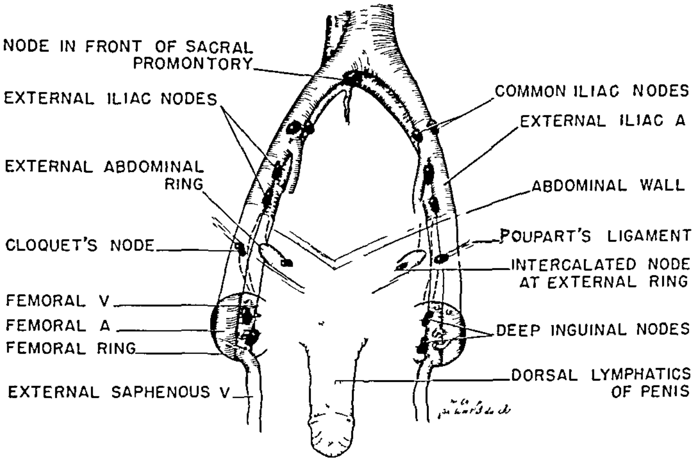

FIG. 1. Lymphatic drainage of penile structures to deep subinguinal and external iliac glands.

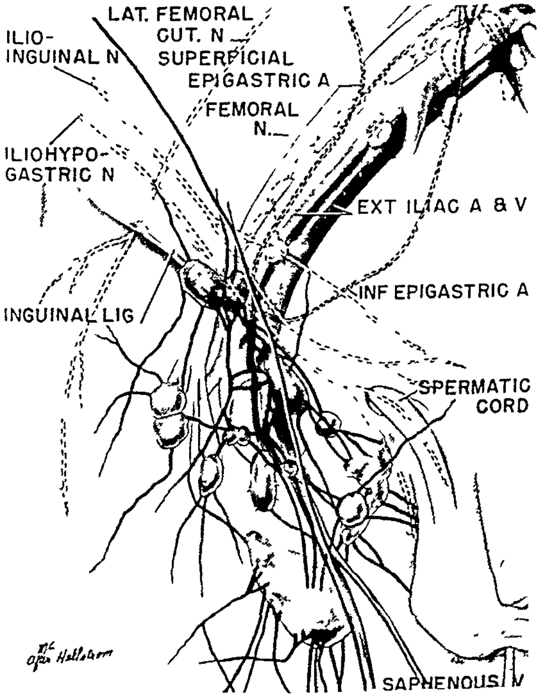

FIG. 2 Anatomic location of superficial inguinal and superficial subinguinal lymph glands.

The external iliac glands are arranged in three groups along the external iliac vessels. One group lies medial another lateral, and the third along the anterior aspect of the vessels. They number eight to ten, and drain the deep subinguinal glands as well as receiving direct channels from the penile urethra and the glans penis (fig. 1). The common iliac glands are situated on the posterior, medial and lateral surfaces of the common iliac artery. One or two glands lie below the bifurcation of the aorta and anterior to the fifth lumbar vertebra. The common iliac glands are four to six in number, and drain the external iliac as well as the hypogastric glands.

Based on these anatomical considerations, the following operative technique has been devised for the treatment of carcinoma of the penis.

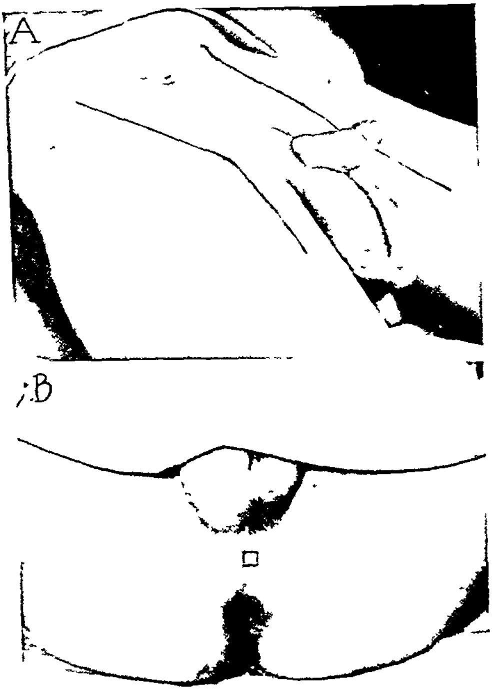

FIG 3 *A*, lines of incision for amputation of penis and bilateral lymph gland dissection. *B*, outline of full-thickness square of skin to be removed at site of urethrostomy.

OPERATIVE TECHNIQUE

A sterile preparation of the operative area is carried out. The portion of the penis involved by tumor is wrapped with sterile gauze to prevent contamination of the wound. A longitudinal incision is made over the symphysis pubis and carried downward to completely encircle the penis at its base (fig. 3, *A*). This incision is deepened until the fascial coverings of the corpora cavernosa and corpus spongiosum are identified. The penile urethra is divided at a point 2 cm. proximal to tumor and freed to a point just beyond the bifurcation of the corpora cavernosa.

The incision circumscribing the penis is extended over the anterior surface of the scrotum. By blunt dissection, the tunics of the testes are separated, creating a pathway to the skin of the perineum. At a point midway between the anterior anal margin and the perineo-scrotal junction, a full-thickness square of skin which measures 1.5 cm. along each side is removed (fig. 3, *B*). This serves to prevent future stenosis at the site of urethrostomy due to contracture of the skin from scar.

The urethra is then delivered through this new orifice and bivalved laterally to produce two flaps. The posterior flap is made shorter than the anterior one. When sutured in place, it serves to direct the urinary stream toward the anus and away from the scrotum.

The corpora cavernosa are dissected back to the pubic rami and divided. Hemostasis is secured by transfixion sutures through the stumps. The scrotum is closed.

An incision is then made from a point 10 cm. lateral to the umbilicus to a point 2 cm. lateral to the pubic tubercle and thence 10 cm. down the anterior surface of the thigh along the course of the femoral vessels. This incision is carried down to the fascia of the external oblique muscle, and to the fascia lata below the inguinal ligament. Skin flaps are raised medially to the midline, and laterally to a line passing longitudinally through the anterior superior iliac spine. All the subcutaneous fat, fascias, lymphatics and blood vessels are removed en masse (fig. 4). When the dissection is complete, there remains only skin above and fascia of the external oblique muscle and fascia lata below. To remove the deep subinguinal glands, the great saphenous vein, cleanly exposed and lying bare from the earlier dissection, is followed to the femoral bulb. The sheath of the femoral vessels is opened and glands lying medial to the femoral vein removed (fig. 5). The femoral ring is explored and the gland of Rosenmuller removed. The muscles of the abdominal wall are traversed by a muscle-splitting incision. The retroperitoneal space is entered and the iliac vessels exposed from the bifurcation of the aorta to the inguinal ligament. The glands and fat about these vessels are removed by sharp dissection under direct vision.

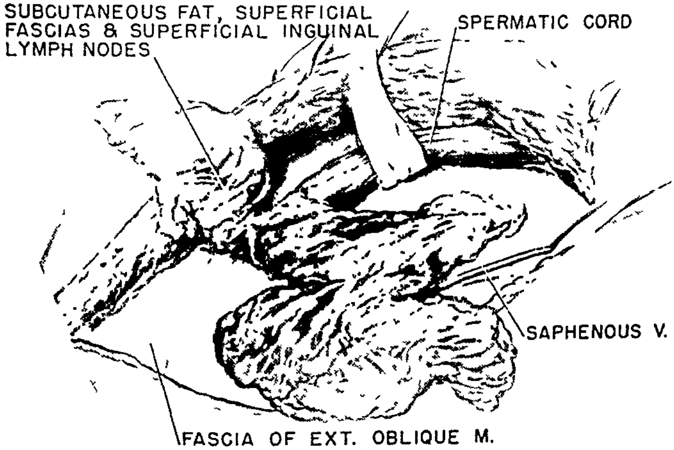
SUBCUTANEOUS FAT, SUPERFICIAL FASCIAS & SUPERFICIAL INGUINAL LYMPH NODES
SPERMATIC CORD
SAPHENOUS V.
FASCIA OF EXT. OBLIQUE M.

FIG. 4 Block dissection of subcutaneous fat and lymphatics of inguinal areas. Spermatic cord and saphenous vein cleanly dissected.

The muscles of the abdominal wall are re-approximated with interrupted sutures. The use of antibiotics, complete hemostasis, careful handling and meticulous closure of the skin, and an adequate sterile compression dressing will contribute much toward the prevention of the loss of skin by necrosis.

CASE REPORT

A 58 year old white railroader was admitted to the Aspinwall Veteran's Hospital August 9, 1951. He stated that he had observed occasional, mild terminal dysuria over the past year. It had never been severe enough to warrant investigation.

On July 24, 1951 the patient noticed some redness and irritation at the tip of his penis. He attributed this original lesion to irritation from his work clothing. The foreskin became edematous and he consulted his family physician. He was hospitalized and treated with local warm compresses. By this time the penis had become markedly swollen, but only moderately painful. The swelling subsided slowly. An urologist was asked to perform a circumcision. His examination resulted in the transfer of the patient to this hospital.

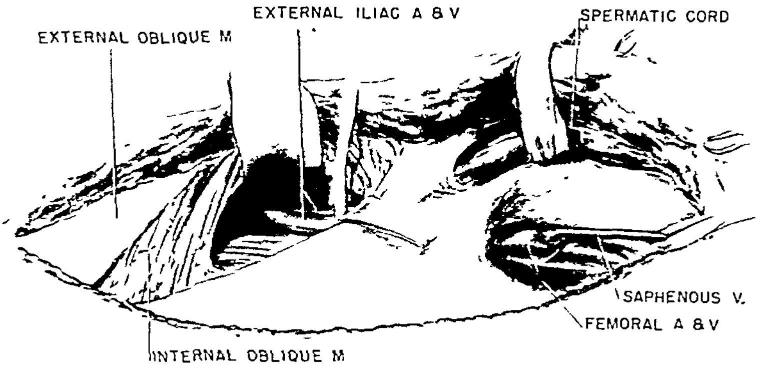

FIG 5. Femoral sheath open and deep subinguinal glands removed. Iliac vessels exposed to aortic bifurcation and lymph glands removed.

The history was remarkable in that the patient had been treated for syphilis in 1941. The serology became negative at the completion of therapy. In April 1951, a repeat serology was doubtful and the patient received a second course of penicillin and mapharsen. It was at the conclusion of this therapy that his present illness developed.

He reported that at the age of 18 an abscess had developed in the right inguinal region which required incision and drainage.

PHYSICAL FINDINGS

The patient was a well developed, well nourished white man of 58 years, who appeared to be in excellent physical condition. The head, neck and chest were not remarkable. The heart and lungs were normal. The blood pressure was 128/76 mm. of mercury. The abdomen was soft and flat. The penis was enlarged

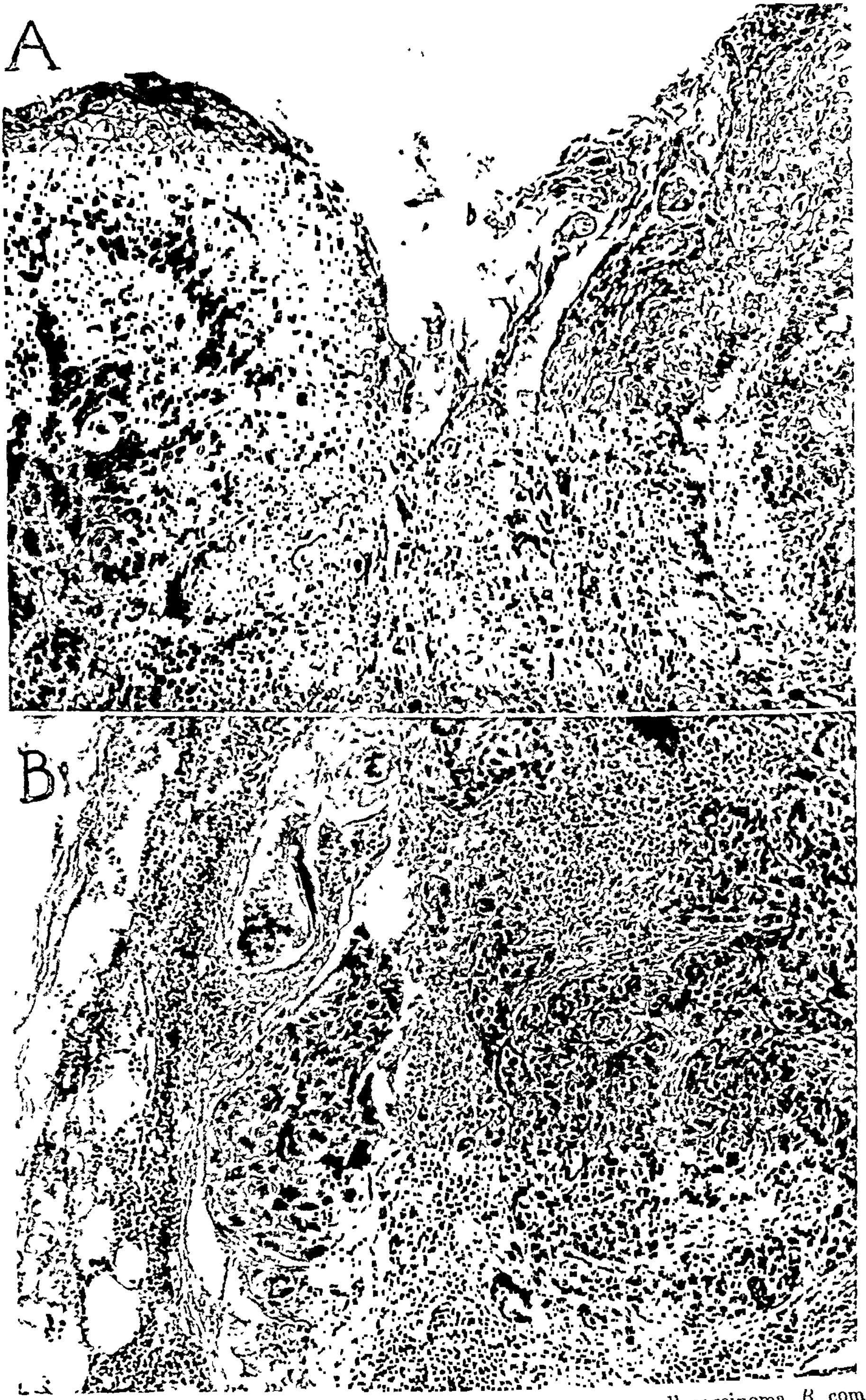

Fig. 6. *A*, photomicrograph of penile lesion. Typical squamous cell carcinoma. *B*, common iliac lymph gland. Note metastatic tumor in subcapsular sinuses and in parenchyma of gland.

and exhibited woody induration over the distal two-thirds. The foreskin could not be retracted. There was no increase in local heat and no tenderness to pressure. The testicles and scrotum were normal. Numerous small, nontender, discrete lymph glands could be palpated in the right inguinal region. The skin overlying the area was scarred. One gland measuring 1 by 2 cm. could be palpated in the left inguinal region. The prostate was normal in size and benign in consistency. The rectal examination was normal.

The x-ray examination of the chest was normal. An excretory urogram demonstrated a normal upper urinary tract. The nonprotein nitrogen and blood sugar were normal. The urine was normal except for 1 plus albumin and the presence of 100 white cells per high power field microscopically. The red count was 4.5 million. The leukocytes were elevated to 15,500 with a shift to the left noted in the differential count.

A presumptive diagnosis of carcinoma of the penis was made on the admission physical examination. A left inguinal lymph gland was removed August 15 and the presence of metastatic squamous cell carcinoma confirmed microscopically. Radical amputation of the penis, perineal urethrostomy, and block dissection of the lymph glands from the bifurcation of the aorta to the level of the apex of the femoral triangle were done August 13 under spinal anesthesia. Because of the length of the procedure, dissection of the glands on the right side was deferred until a later date. Postoperatively, the patient did well. His course was complicated by the breaking down of the skin edges in the area of the inguinal ligament. This was attributed to the extensive undermining of the skin flaps. This portion of the wound healed by secondary intention. The area of slough was not extensive enough to require skin grafting.

On September 13, 1951 a similar block dissection of the lymph glands on the right side was carried out. Again, the postoperative course was smooth. There was some loss of skin edges on this side, but less than occurred on the left.

The lesion of the penis was a squamous cell carcinoma (fig. 6, *A*). There was involvement microscopically of the inguinal, external iliac, and common iliac glands on the right and left sides by metastatic squamous cell carcinoma (fig. 6, *B*).

DISCUSSION

Carcinoma of the penis is by nature a disease of relatively slow progress. This is reflected in the fact that two-thirds of all patients when first seen do not have metastasis to the inguinal regions.[2, 3, 4] This accounts for the high cure rate afforded by simple amputation of the penis.

However, one-third of the patients seen in any large series will have metastatic involvement of the regional lymphatics, and it is the treatment of these with which we are concerned.

Lymphatic drainage of the penis has long been known to go not only to the

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[2] Barringer, B. S.: J. A. M. A., **106:** 21, 1936.

[3] Bassett, J. W.: Personal communication.

[4] Young, H. H. and Davis, D. M.: Young's practice of Urology, Philadelphia and London: W. B. Saunders Co., 1926.

glands of the inguinal regions, but also to the glands along the iliac vessels. In spite of this knowledge, none of the classical radical operative procedures has advocated their removal although the chance of involvement of these nodes by tumor is theoretically equal to that of the superficial inguinal nodes.[5]

It is our conviction that any complete lymph gland dissection must include the glands along the iliac vessels.[6]

The case reported demonstrates that metastasis can and does occur to these glands. Although only the passage of time will determine whether or not a "cure" has been attained in our case, it has been established histologically that anything short of this procedure would have resulted in certain failure.

Many patients who have had penile amputation complain bitterly because they are unable to direct the urinary stream. The act of micturition spills urine over the scrotum and soils the clothing. This operation was successfully designed to provide perineal urethrostomy that would direct the urinary stream in the same line as the fecal stream. Infection, the old bugaboo which once caused even inguinal gland dissection to be approached with fear, is no longer a limiting factor. This operative procedure, although tedious and time consuming, is not technically difficult and is tolerated well by the patient.

Certainly, procedures such as these must be given serious consideration and evaluation by trial if we are to progress in our efforts to increase the survival rate of the unfortunate victims of this disease.

SUMMARY

The lymphatic drainage of the penile structure is described.

It is demonstrated that metastasis to the external and common iliac glands from cancer of the penis does occur.

It is noted that the commonly accepted operative procedures for radical amputation of the penis do not permit the removal of all the lymph glands that may readily become involved with tumor cells.

An operative procedure is presented which provides exposure for an adequate lymph gland dissection, and which can be performed in stages if warranted by the condition of the patient.

The importance of perineal urethrostomy to the comfort of the patient has been brought out.

A case in which this operative technique was performed has been described.

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[5] Young, H. H.: J. Urol., **26**: 285, 1931.

[6] Mendelsohn, S. N. and Mansfield, R. D.: Surg., Gynec. and Obst., **92**: 432, 1951.

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ANATOMY AND TECHNIQUE OF HYDROCELECTOMY

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The technique of hydrocelectomy as employed by us is based on the anatomical dissections illustrated in the popular accepted texts. The drawings in Anson's text are particularly good. In an exterior view of the inguinal region he shows the structural entities of the abdominal wall as they are related to the scrotal structures. It is noted that the skin of the inguinal region is continued to become the specialized skin of the scrotum and the superficial fascia to become the dartos muscle replacing the heavy deposit of fat in the fascia above. The remaining four structures or layers that particularily demand our attention in considering the technique of hydrocelectomy are from within out: the processus vaginalis, internal spermatic fascia, the cremasteric muscle and fascia and the external spermatic fascia. The anatomy and relationship of these are best understood if the embryologic development is followed.

The testicle and the spermatic cord in their descent through the inguinal canal push their way through the transversalis fascia at the abdominal inguinal ring and acquire therefrom an intimate investment, the internal spermatic or infundibuliform fascia. The testicle then encounters the lower border of the internal oblique muscle from which it drags down fibers. This partial covering lying outside the internal spermatic fascia is the cremasteric muscle and fascia. Upon passing through the external oblique aponeurosis, the testicle gains its third outermost covering, the external spermatic or intercolumnar fascia. Thus the testicle and that part of the spermatic cord lying outside the inguinal canal acquire three investments while that part behind the internal oblique has only one, the internal spermatic fascia. Our interest, of course, is primarily concerned with that portion lying without the inguinal canal and its three coverings.

These three funicular coats, in addition to containing the constituents of the spermatic cord (vasa duct and vessels), also contain that very important structure of our study, the processus vaginalis. This, although minute in the normal male individual, is an uninterrupted peritoneal diverticulum from the abdominal orifice of the inguinal canal to its termination at the testis. The process widens when it reaches the testis to almost enclose that organ forming the visceral and parietal layers of the tunica vaginalis. The lack of complete closure of the vaginal process leaves the testis a retroperitoneal organ as it was before descent into the scrotum. Pathologic changes, congenital or otherwise, of or in this vaginal process account for the majority of the various types of inguinal herniae and hydroceles. According to its anatomical location, a hydrocele may be classified as to hydrocele of the testis, hydrocele of the cord, or hydrocele of both the testis and the cord.

THE TECHNIQUE

Based on the above anatomical considerations hydrocelectomy naturally and logically is limited to excision of that portion of the processus vaginalis involved in the cystic deformity. Simply, this means incision through the overlying five layers, careful dissection of the tunica and its excision. If carefully done with due consideration to blood vessel distribution little clamping and ligation need be done, hospitalization limited to 24 to 48 hours and postoperative morbidity such as hemorrhage, infection, swelling and recurrence held to a minimum.

While an assistant immobilizes the scrotal mass a 5 or 6 cm. skin incision is made over the tense mass in line with the prominent vessels seen in the skin. The incision is then carried down through the next four layers, each of which by choice may or may not be dissected separately and recognized. When the tunica vaginalis or hydrocele sac proper is approached it is recognized by its pearly avascular translucent character and ease with which it may be ruptured. In the nonfibrotic case it separates freely from the internal spermatic fascia and need not be ruptured and is delivered through the overlying incision. As the margin between parietal and visceral layers is approached, a heavy network of blood vessels can be noted. By careless dissection these can be torn, followed by hemorrhage necessitating multiple ligations with subsequent edema. If, however, the internal spermatic fascia is carefully separated from the tunica vaginalis, the vessels may be carried with the fascia leaving a near bloodless parietal tunica for excision. The dissection is facilitated by the use of a spatula-like instrument originally intended for eye surgery but adopted by us for this particular procedure. The sac having been delivered, the fluid content is aspirated, opened and the parietal portion excised on a line as it approaches the testis to become the visceral portion of the tunica. No effort is made to remove this structure although a part of the tunica vaginalis. The wound is closed in two layers using 2-0 plain catgut. A small Penrose drain is left in for 24 hours.

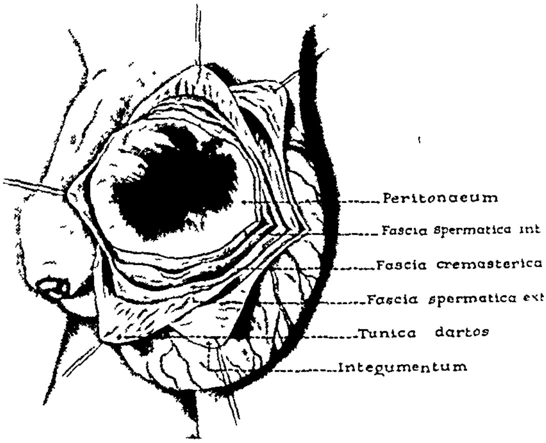

FIG. 1. Illustrating anatomy and technique of hydrocelectomy

Hydrocelectomy of the cord is a much simpler procedure. The approach having been made as aforementioned and the hydrocele visualized, it may be delivered much as the meat of a grape is squeezed from its skin, the base ligated and the cyst excised in toto.

Hydrocelectomy of both the testis and cord would of course utilize both techniques above described.

SUMMARY

A technique of hydrocelectomy based on anatomical logic and very similar to that technique described by Young is presented.

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SCROTAL URETER: REPORT OF A CASE

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In July 1950, a nine year old white boy (BUI 46358) was admitted to the Brady Institute of the Johns Hopkins Hospital for investigation of a hydronephrotic left kidney.

Prior to this he had consulted his local physician because of persistent enuresis and dull right flank pain. Physical examination at that time revealed a large mass occupying the right upper quadrant. Excretory urography disclosed absence of function on the right side, and moderate hydronephrosis on the left. The right kidney was explored elsewhere, and a large hydronephrotic sac removed. After his convalescence, he was referred to the Brady Urological Institute for study and treatment of his left hydro-ureteronephrosis.

Upon admission physical examination revealed scars of well-healed right lumbar and right inguinal herniorrhaphy incisions, and an easily reducible left indirect inguinal hernia. Blood chemical determinations, including nonprotein nitrogen, carbon dioxide combining power, chlorides, and glucose were all reported to be within normal limits. Urinalysis, at this time, showed nothing abnormal, chemically and microscopically. The hemoglobin and white blood cell count were within normal range. The phenolsulfonphthalein test was calculated as 65 per cent excretion in 2 hours. A plain x-ray film of the abdomen showed a moderate sacral spina bifida occulta. Excretory urography confirmed the presence of a marked left hydro-ureteronephrosis with delayed excretion, and lack of filling of the pelvic ureter. Cystogram showed a large conical-shaped bladder without reflux up the left ureter. Because of inadequate visualization of the left pelvic ureter, retrograde pyelography was performed. This film, too, was not helpful, still failing to show the left pelvic ureter. One interesting thing about this film was the pooling of some dye in the region of the left ischiopubic ramus, which, in view of later findings, was diagnostic of the ureteral position. It was ignored as probably representing external spillage. Cystoscopy revealed a normal prostatic urethra and bladder, with no evidence of lower urinary tract obstruction. A No. 4 olivary-tipped catheter passed easily to the left kidney. It was believed that the obstruction must be at or near the ureterovesical junction causing the dilatation of the upper urinary tract. Therefore, this region was surgically explored.

The bladder was opened directly and showed a slightly prominent trigone without hypertrophy. The left ureteral orifice was somewhat snug initially, but was finally easily dilated with a stiff bougie. With the bougie in place, the lower end of the ureter was explored. The lower 5 cm. of the ureter appeared perfectly normal, but above that, as far as could be visualized, it was thick walled, dilated, and tortuous, with no extrinsic evidence as to its cause. Because of its tortuosity,

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Read at annual meeting, Mid-Atlantic Section, American Urological Association, Old Point Comfort, Va. April 14, 1951.

the ureter did not assume the usual smooth curved course to the bladder. Resection of the redundant portion of the ureter was therefore decided upon. After resection of 5 cm. of dilated ureter, and anastomosis of the two ends with 0000 chromic catgut over a 14F T-tube, the ureter seemed to drain well when tested by irrigation. Before closure a wedge was removed from the posterior lip of the vesical neck because of the moderate atonicity of the bladder. The bladder was closed around a suprapubic mushroom catheter.

The suprapubic tube was removed on the fourth postoperative day. On discharge on the fourteenth day, the kidney was draining well from the T-tube into a Davol bag. Blood chemical determinations never varied from their preoperative normal level.

Four days after discharge the patient was re-admitted with fever of 104F. He had no other symptoms, and there was no alteration of the blood chemical analyses. This episode was thought to be caused by a severe urinary tract infection with a transient bacteremia. This responded well to penicillin and streptomycin, and the patient was discharged in ten days, afebrile.

Six weeks later the patient returned for removal of the T-tube. He had been asymptomatic and had been voiding small amounts of urine, although most of it had been passing through the tube. The day after admission a 16F catheter was placed into the urethra. Following this procedure the entire urine output drained through the urethral catheter. Two days following this the T-tube was removed. Excretory urograms, following its removal, showed moderate progression of the hydronephrosis since before the operation. A No. 6 ureteral catheter was then immediately passed with relative ease up the left ureter into the renal pelvis, and was followed first by a gush of urine, and then by constant drops indicative of obstruction. The catheter was left in place and drained satisfactorily for three days. There was another febrile episode which responded well to penicillin and streptomycin. Pursuant to removal of the ureteral catheter a retrograde injection of dye finally revealed the true nature of this boy's condition. After injection of skiodan, the x-ray (fig. 1, *A*) revealed that the catheter entered the ureter at the normal location, but immediately curved downward and looped twice in the region of the scrotal sac, and finally ascended to the renal pelvis. After seeing the film, one could easily palpate the ureteral catheter in the left compartment of the patient's scrotum. It became obvious at this time that nothing had been accomplished by the first operation, and that re-exploration for correction would have to be undertaken.

A curved left lower quadrant incision was made, exposing the inguinal canal. A long loop of dilated ureter was immediately seen extending down into the scrotum. The fascial coverings of the ureter were dissected free and the ureter pulled up from the scrotum. It seemed to be somewhat adherent to the cord structures, but not to the testis. Between the two loops there was what appeared to be a mesentery which contained blood vessels. There was no hernial sac. The lower end of the ureter could be traced down into the pelvis where the previous anastomotic site could be palpated. About 20 cm. of the dilated, redundant thick-walled ureter was then resected, and the cut ends anastomosed over a

T-tube. Without the long redundant loop, the ureter assumed a normal position The T-tube irrigated well both up to the renal pelvis and through to the bladder. The wound was then closed, and the T-tube brought out through a stab-wound. This postoperative course was also uneventful except for slight fever on the fifth and sixth postoperative days. The patient was discharged two weeks later with the T-tube draining well, to return in one month for its removal.

The patient returned after 1 month stating that about equal amounts of urine passed from the bladder as from the tube, and that it had been cloudy on occasions. He had had no untoward symptoms during the intervening period. The tube then was removed, and the patient discharged in good condition after a few days, voiding normally and without external drainage of urine.

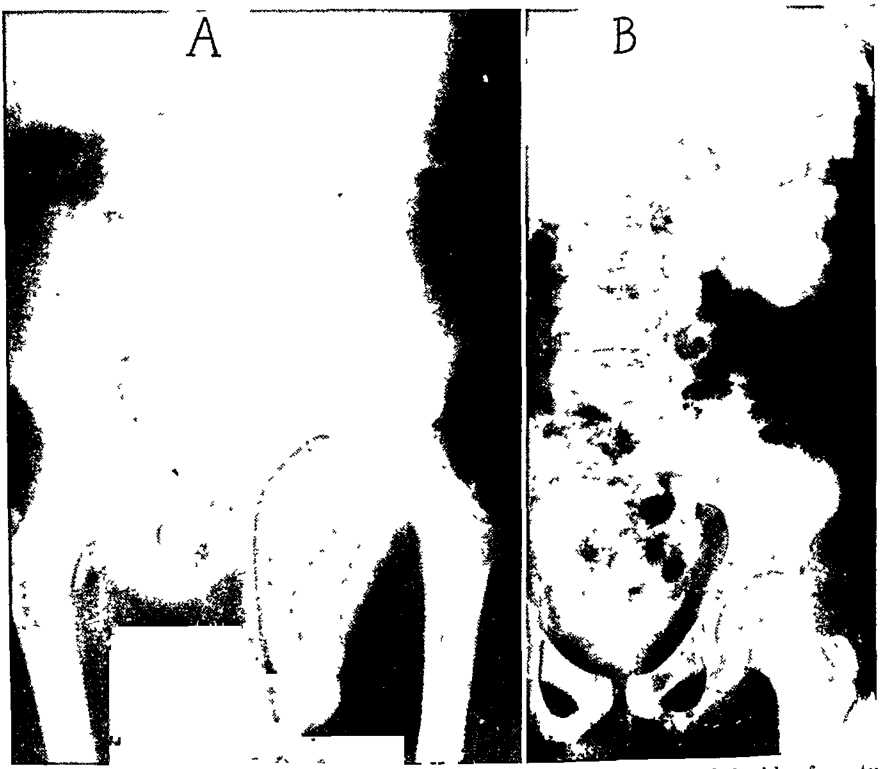

FIG 1. *A*, dilated ureteral loops containing catheter are visualized in left side of scrotum. *B*, obstruction at ureteropelvic junction, as yet untreated, causing persistent hydronephrosis. Rest of ureter is perfectly normal following resection of 20 cm. of herniated scrotal portion and oblique end-to-end anastomosis over splinting T-tube.

During the 5-month period following removal of the T-tube, the patient has been well symptomatically. Recent excretory urograms continue to show a marked degree of hydronephrosis from a still unrelieved obstruction at the ureteropelvic junction, but this is less than that existing at the time of discharge. The ureter is visible, 50 minutes after injection of the dye, all the way to the bladder (fig. 1, B). Its course is normal, and its size is normal, indicating the success of the uretero-ureteral anastomosis. Obstruction at the ureteropelvic junction is to be eliminated during the next admission.

This case is presented as one of a scrotal herniation of the left ureter, undoubtedly congenital in origin. No exact information is obtainable regarding the cause of the dilatation of the right upper tract. It is of interest to note that there was a right inguinal herniorrhaphy previous to the removal of the right kidney. One could speculate that perhaps the same condition existed on the right side as the left, thereby constituting a very rare congenital maldevelopment.

In a review article (*J. Urol.* **38:** 450, 1937) Dourmashkin reported 71 cases of herniation of the ureter: 27 inguinal, 33 femoral, and 11 scrotal. Of the 11 cases of scrotal ureter, six were associated with a hernial sac containing other structures, but only four similar to the case herein presented. In 1 case the variety was not stated. Dourmashkin proposes that this abnormal position of the ureter is the result of its having been drawn into the scrotum by the descending testis during fetal life.

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GANGRENE OF THE SCROTUM AS A COMPLICATION OF RETROPERITONEAL INFECTION

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The unusual condition known as idiopathic scrotal gangrene may result from a variety of causes. These were listed by Whiting as 1) the action of bacteria, either by production of toxins or interference with the blood supply, 2) interference with nutrition by other than bacterial means, 3) mechanical or chemical action, 4) thermal trauma, and 5) injury of the trophic nerves.

Two cases of gangrene of the scrotum have recently been observed at our hospital, both of which presented unusual clinical and postmortem findings, indicating that the condition was secondary to retroperitoneal infection. We are unable to find a reported case in the literature in which a similar etiology is described

CASE REPORTS

Case 1. An elderly white man was admitted in a semicomatose state. No history was available. Essentials of the physical examination: temperature, 102F; pulse, 120; blood pressure, 94/72. Mouth: tongue and mucous membranes were dry. Chest: clear to auscultation and percussion. Heart: tachycardia, rate regular, no murmurs or thrills. Abdomen: marked tenderness, especially on the right side, moderate distention, rebound tenderness in the right lower quadrant. Genitalia: swelling and gangrene of the lower portion of the scrotum and a small right inguinal hernia.

Laboratory data: white blood cells, 6,900, hemoglobin, 97 per cent. Blood sugar, 115 mg per cent; nonprotein nitrogen, 114 mg. per cent; creatinine, 13 mg. per cent; total protein, 9.6 mg. per cent. Urine: alkaline in reaction, specific gravity, 1.017, albumin 3 plus, sugar negative, loaded with amorphous sediment, few pus cells; benzidine test was positive; no casts were seen.

Clinical impression: 1) right strangulated inguinal hernia; 2) possible torsion of the testicle.

Progress: A right inguinal incision was made and a small indirect hernia was observed. The cord structures were gangrenous to the internal ring. There was a wide excision of the gangrenous tissue, with removal of the right cord and testicle. The patient was returned to the ward in poor condition and expired 12 hours later. A culture taken at the time of surgery showed Escherichia coli, Proteus fecalis, and a hemolytic staphylococcus albus. No anaerobic cultures were made.

Autopsy findings: The peritoneum contained approximately 400 cc cloudy straw-colored fluid. There was no exudative peritonitis. A ruptured appendix was retrocecal in position and had caused an intense, necrotizing inflammatory reaction in the retroperitoneal tissues, extending forward along the lateral wall to the internal inguinal ring and following along the spermatic cord downward into the scrotum. A correlation of the autopsy findings with the findings of the surgical specimen indicated that the inflammatory process had followed along the

Read at annual meeting, South Central Section, American Urological Association, Houston, Texas, October 29, 1951.

cord and involved all layers but was confined within the limits of the external spermatic fascia. The testicle and epididymis were not gangrenous, but the subcutaneous scrotal tissues were involved in the gangrenous process. There was a septic thrombosis of one of the large veins of the pampiniform plexus.

Final diagnosis: Ruptured acute gangrenous appendix (retrocecal) with retroperitoneal para-appendiceal abscess and gangrene extending into the scrotum.

Case 2. A white man, aged 38, had been drinking approximately 1 quart of whiskey a day for the past 12 days. Four days before admission there was gradual onset of pain in the lower abdomen. The following day the pain was more severe and a private physician was called, who advised hospitalization. The physician reported that there were no positive physical findings at this time. The patient refused hospitalization, stating that he had had previous attacks from which he had always recovered following the use of enemas. On the morning of admission, 2 days later, at 5:00 a.m., he was awakened by a severe pain in the abdomen, with abdominal distention associated with profuse perspiration. His wife noticed swelling of the scrotum at this time. The physician was again called, who insisted upon hospitalization.

Physical examination showed a well-developed and nourished white man, acutely ill, in shock, with cold skin, profuse perspiration, and very apprehensive. Eyes: pupils dilated. Mouth: poor oral hygiene. Chest: bronchial vesicular breath sounds, no dullness. Abdomen: marked distention; generalized tenderness; no hernia. Rectal: liquid feces of a light yellow color. Prostate: not unusual. Scrotum: swollen, with a bluish discoloration.

Laboratory data: white blood cells, 12,500; hemoglobin, 88 per cent. Blood sugar, 297 mg. per cent; creatinine 7.8 mg. per cent; nonprotein nitrogen, 72 mg. per cent; chlorides 435 mg. per cent; carbondioxide combining power, 60 vol. per cent; calcium, 6.5 mg per cent; phosphorus 5.4 mg per cent. Urine: acid in reaction, showed a trace of albumin, with 15–20 white blood cells and 10–12 red blood cells per high power field.

The patient continued in a state of shock in spite of supportive therapy and expired 12 hours after admission.

Essential autopsy findings: The abdomen was distended and tympanitic; there were no scars or striae. The scrotum was swollen approximately four times its normal size, was edematous, more firm in consistency than usual edematous tissue, and was a light bluish-brown color. The penis was not unusual. There was a small amount of dark reddish brown fluid in the peritoneal cavity and there was a butyric acid odor. The gastrohepatic ligament was firm in consistency and had a brownish purple color. A similar reaction was present beneath the posterior peritoneal wall, extending upward into the mesentery of the small bowel. The process was more intense in the area of the pancreas and extended both upward and downward, as well as laterally, into the gutters. The appearance was generally the same, being a purplish-brown color, firm in consistency, and covered with spotty areas of fat necrosis that were whitish to grayish-yellow in color. The process extended upward and involved both the anterior and the posterior boundaries of the foramen of Winslow, laterally and downward in the retroperitoneal space. On the right, it extended behind the cecum but did not extend into the pelvis. On the left, it extended down the gutter and into the mesentery of the descending and sigmoid colon. It followed the spermatic artery downward and involved the left spermatic cord. The subcutaneous tissues of the entire scrotum were involved in the same gangrenous process. The left testicle was not involved. There was a small amount of fluid in the tunica vaginalis on the right. The epididymis was tense and was brownish-purple in color. This process was confined to the limits of the cord by the external spermatic fascia, and did not involve the subcutaneous tissue over the inguinal canal. Microscopic studies confirmed the gross postmortem findings.

Diagnosis: 1) Acute hemorrhagic pancreatic fat necrosis; 2) acute peripancreatic and retroperitoneal fat necrosis, with extension of the necrosis into the mesentary, lateral gutters, and into the scrotum.

COMMENT

The anatomical basis for this spread of the gangrenous process from the retroperitoneal space becomes apparent when one remembers that the processus vaginalis traversing the inguinal canal carries with it a layer of the transversalis fascia and the external oblique muscle. These are the internal and external spermatic fascia which form a sheath about the cord until it reaches the upper part of the tunica vaginalis, where it disappears in the subcutaneous tissue of the scrotum. The patent processus vaginalis atrophies, leaving the tunica at its distal end with a fibrous cord extending from the upper portion of the sac to the peritoneum. The retroperitoneal tissue is continuous through these two tubular fascial structures with the subcutaneous tissue of the scrotum. Following this route, any retroperitoneal process would first make itself apparent in the subcutaneous tissues in the scrotum. It would then extend upward toward the lower portion of the abdominal wall and thereafter follow the course of extravasated urine.

A search of the literature since 1905 fails to yield reports of a similar type of spread. That such anatomical boundaries do exist has been demonstrated by Schuller, Bell, Counseller and Butsch. These authors report surgical emphysema of the scrotum following operations on the kidney, in which the air had traveled along the retroperitoneal space into the scrotum. Counseller and Butsch present x-ray plates showing the air in the retroperitoneal tissues, in the inguinal canal and in the subcutaneous tissue of the scrotum. Bell states that in such a condition the scrotum may attain the size of a football.

Because our cases were similar to the reported instances of "idiopathic scrotal gangrene," a correlation of clinical and pathological findings of our cases and those reported in the literature was attempted. The first review of these cases was made by Whiting in 1905. In 1920, Randall presented 16 new cases. In one of these, case 8, the onset of the scrotal gangrene occurred 9 days after the onset of the illness. In this case there was vomiting and abdominal distention with tenderness. The case ended fatally, but no autopsy was reported. We believe this could have been a case of retroperitoneal infection, with subsequent involvement of the scrotum. In the other cases presented by Randall the patients recovered, or presented no abdominal findings.

Gibson reviewed 206 cases in 1930. There are no autopsy findings reported except in one case presented by Gibson himself, in which no retroperitoneal lesion was found. In this entire series of 206 cases, no mention was made of an extension of a retroperitoneal infection into the scrotum.

Since Gibson's report, 14 more cases have been added. Castle reported a case with fatal termination, without autopsy findings. Brunn and Ferris reported a case of idiopathic scrotal gangrene, which occurred 6 days following an appendectomy. This patient presented a course which was typical of idiopathic scrotal gangrene with recovery. We believe that in this case there is a possibility that the scrotal infection was the result of a retroperitoneal inflammatory process. Other cases have been reported by Linder and Levitas, Gorowitz, Brown and Smith, and Shafiroff, in which the lesion followed a circumcision. Rose presented 2 cases; the first followed a typical course; the second followed a known case of pyelonephritis and cystitis. There is a possibility that this case may have resulted from retroperitoneal infection. Howard reported a case and detailed a method of plastic surgery repair. Marchildon reported 2 cases with recovery. Bertoglio and Ratliff reported 2 cases of gangrene of the scrotum with previous urethral disease. Mansfield reported a case with recovery.

In none of Gibson's 206 cases, or the 14 subsequently reported, has mention been made of scrotal gangrene resulting from a retroperitoneal infection. Our 2 cases clearly demonstrate extension of a retroperitoneal gangrenous process into the scrotum with resultant scrotal gangrene. We believe there is adequate anatomical basis for such an extension. It is possible that many cases of so-called idiopathic scrotal gangrene could have resulted from a retroperitoneal infection as indicated in the various case reports, but either the absence of autopsy findings, or recovery of the patient probably explains the fact that no previous similar etiology has been reported. We do not offer this as the only obvious etiologic mechanism by which scrotal gangrene occurs, but wish to emphasize that retroperitoneal infections must be considered in the differential diagnosis of this condition.

SUMMARY AND CONCLUSION

Two cases of scrotal gangrene are reported associated with a retroperitoneal gangrenous process. A short anatomical description of the inguinal region is given, showing the possibility of spread from the retroperitoneal space into the scrotum. We cannot find, in a review of the literature of "idiopathic scrotal gangrene," mention of retroperitoneal infections as a possible causative factor, but three of the reported cases suggest such a retroperitoneal infection to us. It is believed that retroperitoneal lesions must be included in the differential diagnosis, when gangrene of the scrotum develops.

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SOLITARY RENAL CYSTS

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Solitary cysts of the kidney are encountered infrequently in the average clinic, although the literature contains a number of reports on this type of renal lesion. Recently, the head pathologist at one of our large medical schools informed us that he had not seen a case of solitary renal cyst at the autopsy table for the past two years. Prior to 1926, Young found no case of simple renal cyst in 12,500 admissions to the Brady Urological Institute. Later, Fish diagnosed 32 cases in 12,000 urological admissions. At the Brady Foundation in the New York Hospital 18 cases of simple cysts were reported between the years of 1921 and 1943. In four of these, more than one cyst was present in the affected kidney. Hepler, in 1930, collected 249 cases from the literature. Of these, 212 cases were serous cysts and the remaining hemorrhagic. To this group he added seven of his own, four serous and three hemorrhagic. Simple cysts of the kidney are more frequently diagnosed today because of the improvement in our methods of preoperative study and the fact that the urologist has the possibility of such a condition in mind.

Solitary cyst of the kidney must be distinguished from polycystic disease as well as specific cystic conditions of the kidney such as hydatid disease, dermoid cysts and cystic degeneration of tumor. It must also be distinguished from hydrocalycosis in which a cyst-like cavity is found which communicates with the pelvis by a narrow opening.

The true solitary cyst is generally found in the renal cortex and usually the greater part projects from the surface of the kidney. Less commonly, the cyst may be in close relationship with the renal pelvis. These cysts may vary from 1 cm. in diameter to an enormous size such as one reported by Carling in 1934 which contained over 25 pints of fluid.

The cyst wall is generally composed of fibrous tissue lined with a single layer of flat endothelium, but in the larger cysts, the endothelial lining is frequently absent over many areas. These large solitary cysts are most commonly found at the poles of the kidney, the lower pole being a more common site than the upper. This may be accounted for, in part, by the fact that those located at the lower pole of the kidney are more easily diagnosed, as the cyst wall can occasionally be observed in a film of the kidney.

The cyst contents are usually simple serous fluid, though at times one may find blood. The hemorrhagic cyst is often considered evidence of malignant degeneration or associated with a renal neoplasm. This is so in about 30 per cent of the cases, but in only 2 per cent, where the cystic contents are not bloody, are they malignant. Many of these cases are associated with other renal lesions, the most frequent being chronic nephritis and the least common tuberculosis.

Read at annual meeting, Mid-Atlantic Section, American Urological Association, in Philadelphia, Pa., April 19, 1952.

While hematuria is one of the common findings in tumor of the kidney, and reported by Hinman and Howes as the initial clinical manifestation in approximately 40 per cent of patients suffering from this disease, it is interesting to note that it occurs much less frequently in the presence of serous cysts of the kidney. Braasch reports that gross hematuria was noted in 13 per cent of his series of cases, but he believes that associated renal lesions caused the hematuria in some cases. In Prather's experience with solitary cysts of the kidney, gross hematuria was a rare symptom and microscopic hematuria infrequent. It appears from a review of the literature that gross hematuria is far less common in solitary cyst of the kidney than in renal malignancy.

The etiology of solitary cysts of the kidney is a subject of considerable controversy and many authorities frankly admit that the cause is undetermined. There are two schools of thought, however, one favoring the congenital origin on the same basis as that used to explain polycystic disease but with only one tubule being involved in the formation of the cyst. A second group favors an acquired etiology since it is rather common knowledge that these cysts appear in later life at a time when one is more apt to find organic disease of the kidney in which scarring and other damage have occurred. Some emphasize interference of the blood supply; others, obstruction to the tubules as a primary mechanism of cyst formation; but all agree that the lesions are secondary to some previous organic disease.

We herewith present 3 cases of solitary cyst of the kidney admitted to the Atlantic City Hospital within the space of three months.

CASE REPORT

Case 1. A 44 year old white man was admitted to the hospital on June 14, 1951 with the complaint of intermittent right upper quadrant and epigastric pain of 6 years duration. The pain was dull and radiated to the right costovertebral angle and the right shoulder. It was not relieved by analgesics but there was some relief obtained by assuming the recumbent position, except when lying on the right side. Activity aggravated the discomfort. Attacks lasted a week or two and occurred at intervals of 2 or 3 months. No other symptoms referable to the genitourinary tract were present. The remainder of the history was noncontributory.

Physical examination was negative except that the blood pressure was 160/80 and tenderness was present in the region of the right kidney on bimanual palpation and fist percussion at the costovertebral angle. The laboratory tests were entirely negative including urinalysis. Because of the location of the pain, a gall bladder study was made which proved negative. Excretory urograms suggested a space occupying mass in the right kidney and a retrograde study confirmed this finding (fig. 1).

At operation, the right kidney was exposed through the usual flank incision. A large cyst was found protruding from the midportion of its convex border (fig. 2). Straw colored fluid was obtained by aspiration, following which the free portion of the cyst was excised. The cyst extended deeply into the parenchyma, practically bisecting the kidney, but there was no communication with the pelvis. The intrarenal portion of the cyst wall was cauterized with 50 per cent

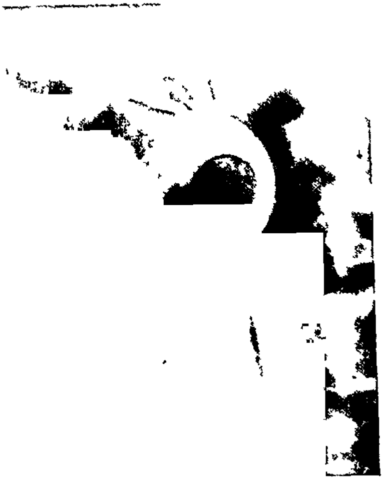

FIG. 1. Case 1. Preoperative right retrograde pyelo-ureterogram showing moderate deformity of middle calyx with normal true pelvis.

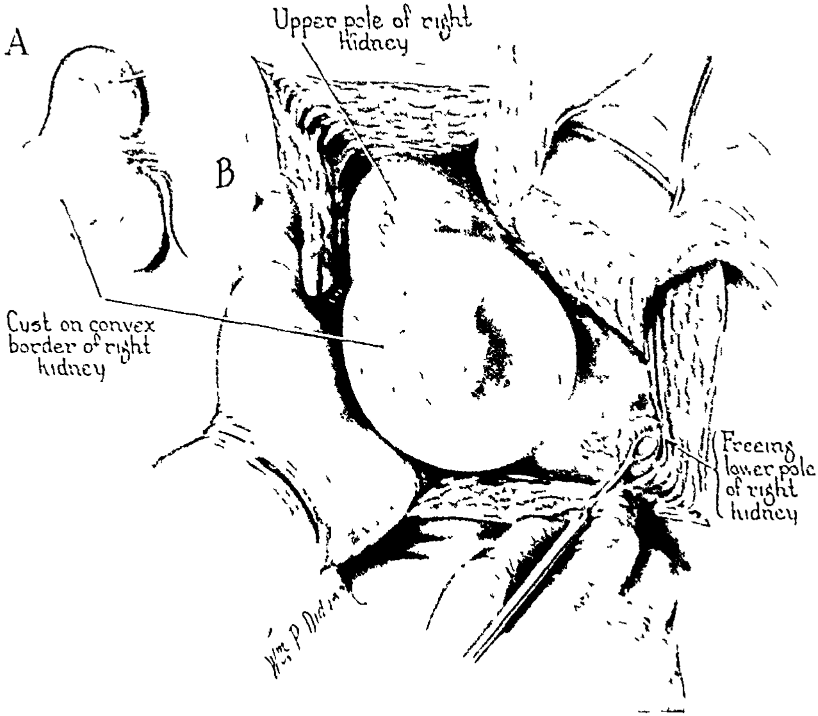
A
B
Upper pole of right kidney
Cyst on convex border of right kidney
Freeing lower pole of right kidney
Wm P Didusch

FIG. 2. Case 1. Gross appearance of cyst protruding from external border of right kidney in its midportion.

phenol in glycerine and neutralized with 95 per cent alcohol. The cavity was filled with fat and closed with a series of single sutures through the renal capsule and parenchyma (fig. 3). The kidney was replaced in its bed and the wound was closed in layers with drainage.

Histological study of the excised cyst wall revealed that it was composed of dense connective tissue and lined with flattened endothelial cells. Occasionally one may see elements of renal tubules with hyaline casts. There was no evidence of malignancy (fig. 4). The fluid from the cyst was clear and straw colored. It was alkaline and the sediment contained 30–40 red blood cells and 0–2 white blood cells per high powered field after centrifugation. Four Papanicolaou smears of the centrifuged sediment revealed no malignant cells.

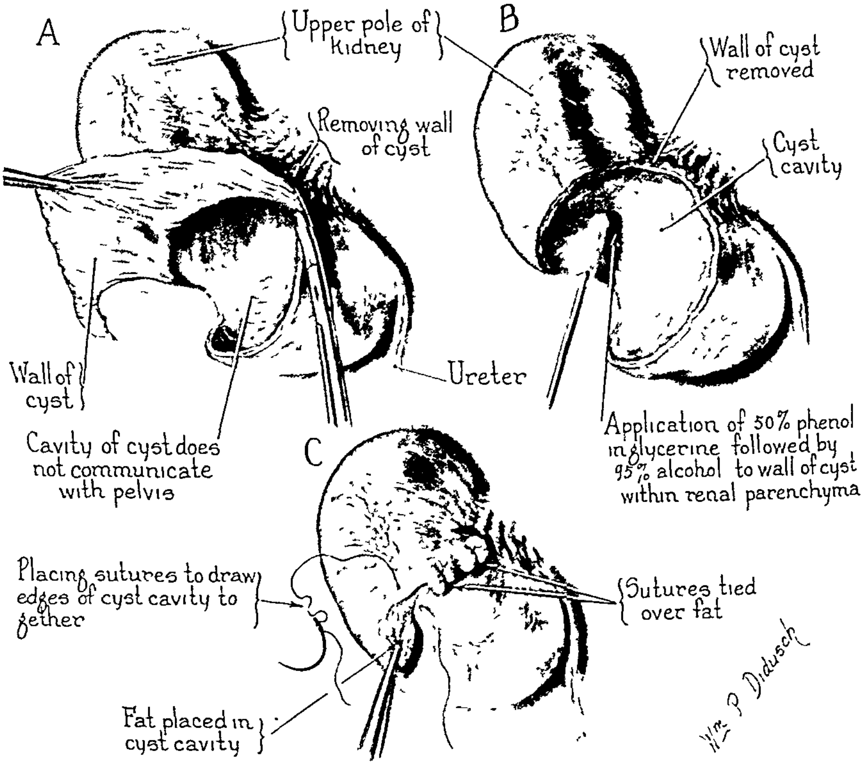
A
Upper pole of Kidney
B
Wall of cyst removed
Removing wall of cyst
Cyst cavity
Ureter
Wall of cyst
Cavity of cyst does not communicate with pelvis
C
Application of 50% phenol in glycerine followed by 95% alcohol to wall of cyst within renal parenchyma
Placing sutures to draw edges of cyst cavity together
Sutures tied over fat
Fat placed in cyst cavity

FIG 3 Case 1. Free portion of cyst wall being excised with cauterization and repair.

The patient made an uneventful recovery and was discharged ten days after the operation with a blood pressure of 120/70. He was entirely asymptomatic with a normal right pyelo-ureterogram (fig. 5).

Case 2. A 62 year old white man was admitted to the Atlantic City Hospital for operation on Agust 10, 1951 with a diagnosis of solitary cyst of the left kidney. Four years prior to this admission, he had had an attack of hematuria following an appendectomy. Studies at that time revealed the presence of what was thought to be a cyst of the left kidney, but the patient refused surgery. A recent urological work-up confirmed the original diagnosis of a grapefruit sized mass attached to the lower pole of the left kidney (fig. 6, *A*).

Physical examination on admission revealed nothing unusual except some increase in the blood pressure, which was 160/100, with a grade 2 sclerosis of the

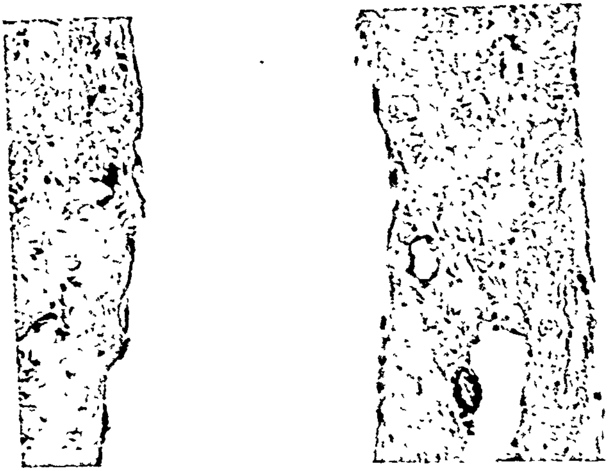

Fig. 4. Case 1. Photomicrograph of cyst wall showing remains of flattened endothelial cells lining inner wall. ×120.

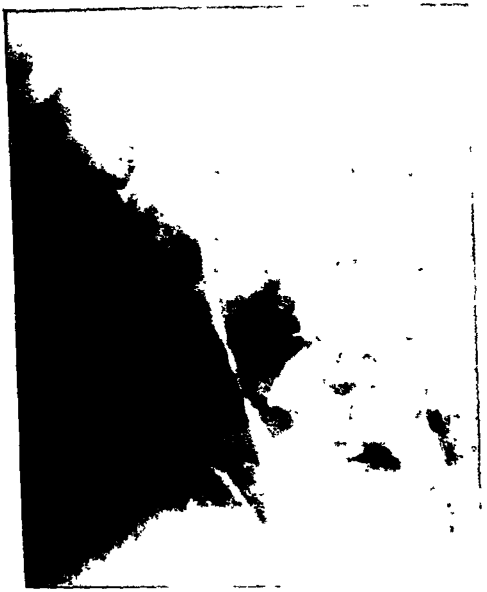

Fig. 5 Case 1. Postoperative retrograde right pyelo-ureterogram showing normal renal pelvis.

retinal arteries. The laboratory tests were all entirely negative with the exception of a few red blood cells in the urine.

At operation, the left kidney was exposed through the usual flank incision and completely freed. A large grapefruit sized cyst protruded from the anterior surface of the lower pole. A clear, amber colored fluid was aspirated. The free portion of the cyst wall was excised. There was no communication with the pelvis. The cut edge of the cyst wall was attached to the true capsule of the kidney with a continuous suture of No. 00 chromic catgut. The intrarenal portion of the cyst wall was cauterized with 50 per cent phenol in glycerine followed by neutralization with 95 per cent alcohol. Histological study of the excised membrane revealed that it consisted of hyalinized connective tissue with an occasional atrophic renal tubule. After centrifugation, the sediment of the cyst fluid contained an occasional polymorphonuclear leukocyte. There was no evidence of malignancy.

The postoperative course was uneventful. The patient was discharged on the eleventh postoperative day; the blood pressure was 136/94, which was an improvement over the preoperative level of 160/100. The cyst was so located that it may have interfered with renal circulation. Except for the absence of the cyst shadow in the x-ray film, there is very little difference between the preoperative and postoperative appearance of the left renal pelvis; however, we believe that there is less dilatation of the inferior calyx in the latter (fig. 6, *B*).

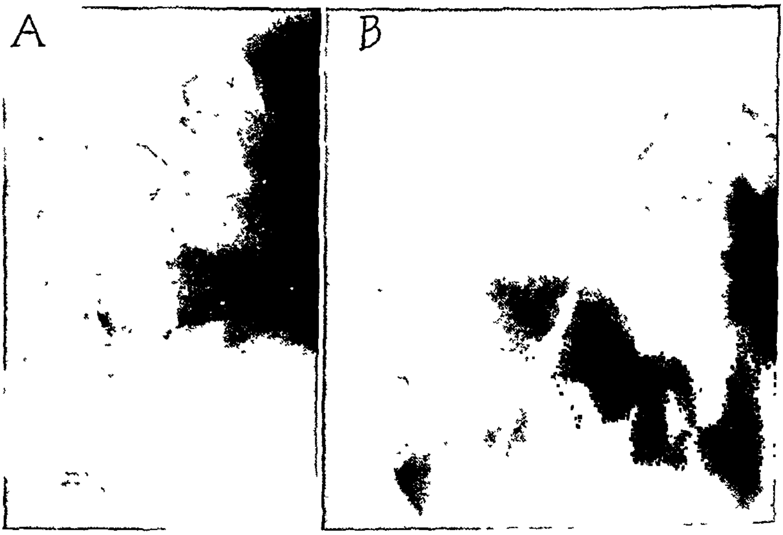

FIG 6. Case 2. *A*, preoperative pyelo-ureterogram showing location of cyst on anterior surface, lower pole of left kidney, with some broadening of inferior calyx due to pressure. No deformity of true pelvis. *B*, postoperative left pyelo-ureterogram showing more normal lower major calyx.

Case 3. A 56 year old man was admitted to the Atlantic City Hospital on August 1, 1951 with a history of prostatism of 3 months duration. He was subjected to our routine preoperative studies which we employ in prostatic cases. An excretory urogram suggested a mass lesion in the lower pole of the left kidney. Cystoscopy revealed a diffuse cystitis but no significant degree of obstruction of the vesical neck. There was no residual urine. Retrograde pyelograms substantiated the finding of a definite space occupying lesion in the lower pole of the left kidney (fig. 7). Upon close questioning, he now admitted that for many years he had experienced left upper quadrant discomfort which had been ascribed to a psychoneurotic tendency.

Physical examination was completely normal. The blood pressure was 102/60.

FIG. 7. Case 3. Preoperative left pyelogram showing some deformity of calyces suggesting space-occupying mass with no impingement on renal pelvis

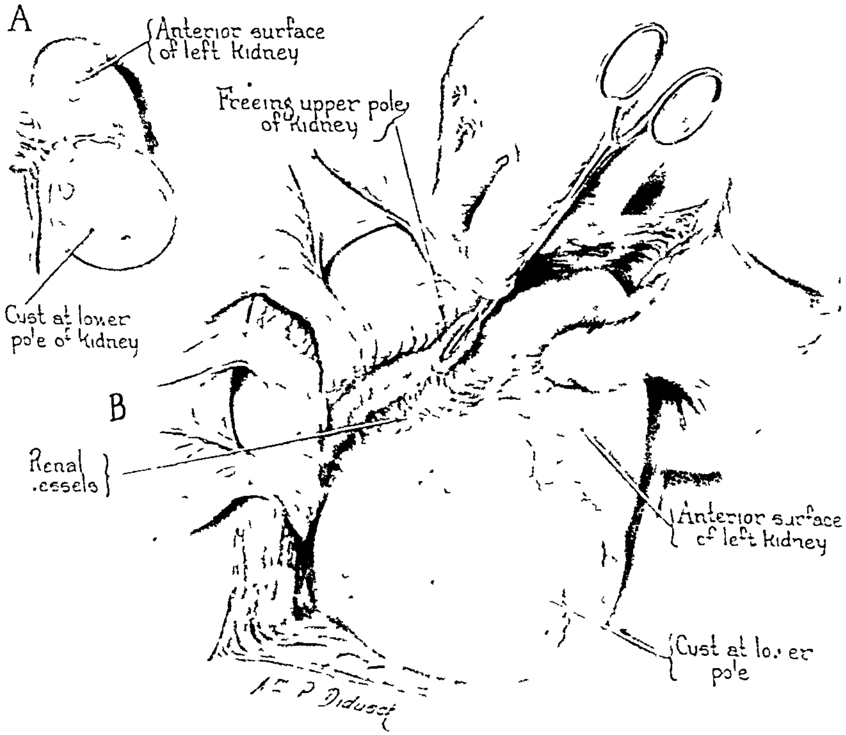
A
Anterior surface of left kidney
Freeing upper pole of kidney
Cyst at lower pole of kidney
B
Renal vessels
Anterior surface of left kidney
Cyst at lower pole
Didusch

FIG. 8. Case 3. Gross appearance of cyst occupying anterior surface of lower pole of left kidney

No abdominal masses were palpable and no costovertebral angle tenderness. Rectal examination revealed a small benign prostate. Laboratory findings were all within normal limits except for the urinalysis which revealed a heavy infection with Pseudomonas aeruginosa.

The kidney was explored through the usual flank incision. A grapefruit sized cyst protruded from the anterior surface of its lower pole (fig. 8). After aspirating serous fluid, the free portion of the cyst was excised. The cyst extended toward the hilum but did not communicate with the pelvis. The cut edge was sutured *with a continuous suture of No. 00 chromic catgut.* The remainder of the cyst wall was cauterized with 50 per cent phenol in glycerine and neutralized with 95 per cent alcohol (fig. 9). The kidney was replaced in its bed and the wound closed in layers with drainage.

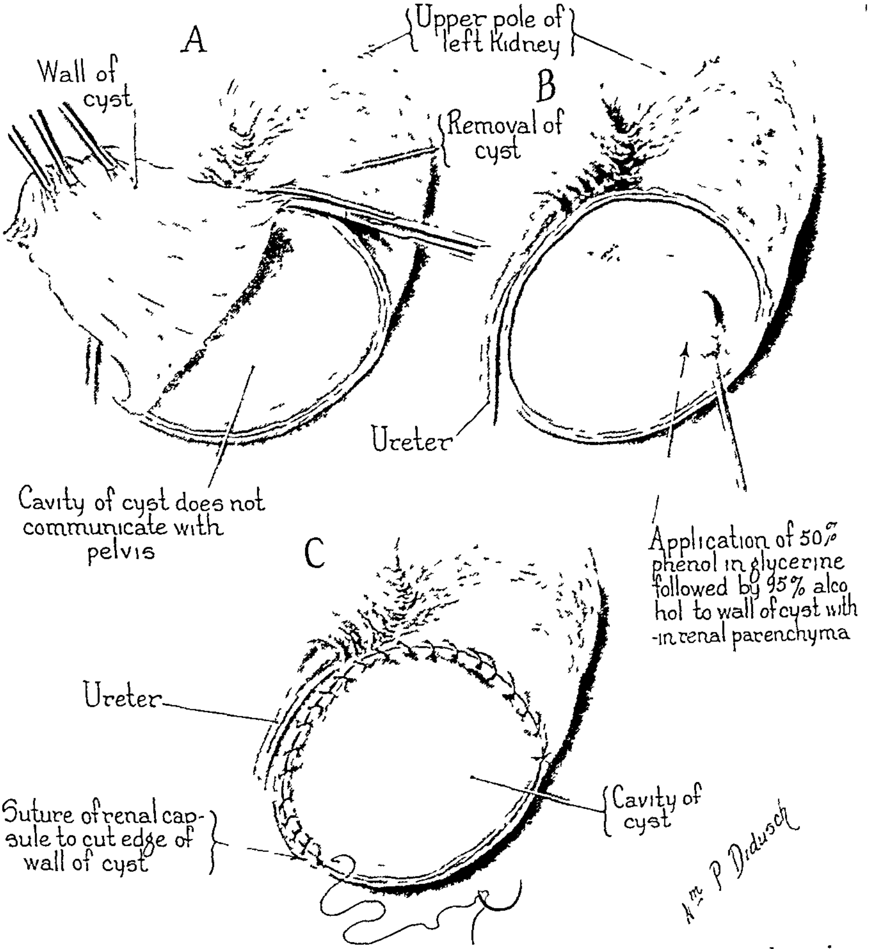
A
Wall of cyst
Upper pole of left Kidney
B
Removal of cyst
Ureter
Cavity of cyst does not communicate with pelvis
C
Application of 50% phenol in glycerine followed by 95% alcohol to wall of cyst with -in renal parenchyma
Ureter
Suture of renal capsule to cut edge of wall of cyst
Cavity of cyst
Wm P Didusch

FIG 9 Case 3 Excision of free portion of cyst wall with cauterization and repair

Histological study of the cyst wall revealed hyalinized connective tissue with a few thick walled blood vessels and scattered remnants of renal tubules. *Papanicolaou stain on the sediment of the cyst fluid* revealed no malignant cells.

The patient made an uneventful recovery and was discharged eleven days postoperatively. The left upper quadrant abdominal symptoms formerly present disappeared following the operation and have not recurred to date. A postoperative pyelo-ureterogram revealed a normal pelvis (fig. 10).

There was no evidence of impaired renal function in the three cases reported. In fact, in two, the divided quantitative specimens showed a larger percentage of dye excreted by the kidney containing the cyst.

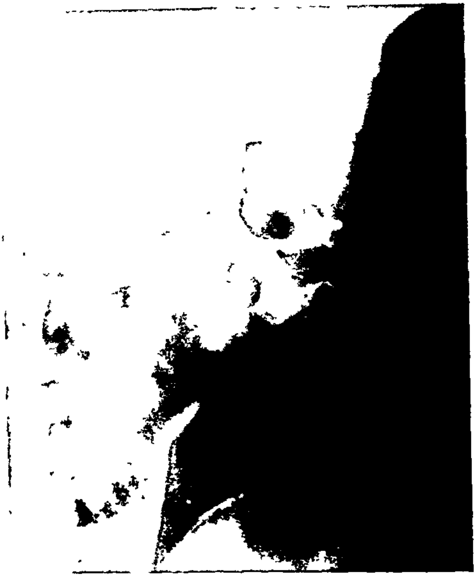

Fig. 10. Case 3. Postoperative pyelo-ureterogram demonstrating normal left renal pelvis.

DISCUSSION

As one can see, in regard to symptoms, there is no definite clinical pattern. The symptoms produced by any particular cyst depend chiefly on its location and the degree of pressure, if any, which it exerts on the renal parenchyma, pelvis, calyces, ureter or other abdominal organs. Many of the cases give no symptoms whatsoever, the lesion being discovered during a routine examination of the upper urinary tract.

Of the 3 cases we have reported, it is interesting to note that the only one having significant subjective symptoms was the one in which the cyst was found protruding from the lateral border of the kidney. We believe from its size and location that it exerted a greater amount of intrarenal pressure. To explain some of the symptoms complained of by this patient, we became interested in the innervation of the kidney and found that the sensory nerve fibers enter the cord with the tenth, eleventh and twelfth thoracic nerves and one would assume that the sensory findings from intrarenal pressure would be referred to the areas supplied by these nerves; that is, the lower thorax and upper abdomen. However, we could not explain the pain in the shoulder on the basis of the renal innervation.

The physical examination is most important. One can sometimes palpate a mass in the region of the kidney. If the kidney is freely movable, its size, contour and consistency can be more accurately estimated, but it is most difficult to decide between tumor and cyst. X-rays and pyelograms are the greatest aid in determining the presence or absence of a tumor mass in the kidney and in differentiating between a malignant tumor and a solitary cyst. A plain film of the abdomen will determine the size, shape and location of the kidney and in some instances, the outline of the cyst wall. However, occasionally these rounded outlines projecting from the renal mass and taken to be cysts in the preoperative study may subsequently prove to be tumor.

Calcification in renal cyst is not common, although our last case (not included in this series) showed a small area of calcification in the region of a large cyst occupying the upper pole of the kidney.

In regard to the value of excretory versus retrograde pyelograms, we feel that both play an important part in the diagnosis and should be used routinely. As a rule, the retrograde study is more informative, although occasionally a urogram will give information which cannot be obtained by the former procedure.

In our limited experience with solitary cysts of the kidney, we have noted that there has never been the obliteration of the calyces nor deformity of the true pelvis commonly seen in tumor of the renal parenchyma. Our pyelograms have shown principally deformity, consisting of dilatation, displacement or flattening of the calyces. We are cognizant of the fact, however, that both tumor and cyst of the kidney are space displacing lesions and that either one, in the proper location and of sufficient size, might cause pelvic deformity.

We do not wish to leave the impression that the differential diagnosis between malignant tumors and solitary cysts of the kidney can be made in the average case preoperatively, although we believe that in the presence of a solitary cyst, there is less likelihood of a deformity of the true pelvis.

SUMMARY

Various aspects of solitary renal cysts have been discussed. We have presented three cases emphasizing the symptomatology, differential diagnosis and surgical treatment of this entity.

We wish to express our sincere appreciation to the artist, Mr. William P. Didusch, for the beautiful illustrations which accompany this paper.

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ARTERIOVENOUS FISTULA OF THE RENAL VESSELS: CASE REPORT AND REVIEW OF THE LITERATURE

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The purpose of this paper is to present the fourth proven case of arteriovenous fistula of the renal vessels. It is the first case recorded wherein the fistula formation was due to neoplastic infiltration.

CASE REPORT

A 29-year old white male Army officer was admitted to Brooke Army Hospital on September 19, 1950 with the chief complaints of cough, recurrent headaches, mild difficulty in breathing and fatigue. He was transferred from a nearby Army hospital with the diagnosis of Boeck's sarcoid of the lung, and hypertension, cause undetermined.

His present illness began in the spring of 1950 when the patient noted the gradual onset of fatigue, listlessness and lack of ambition. At this time, he began having high frontotemporal headaches. In May 1950, he first noted a dry hacking cough with some difficulty in taking a deep breath. He was treated symptomatically by his dispensary physician and in August 1950 he had a more acute episode of dyspnea with a "whistling" in his chest. At this time, examination revealed an elevation of blood pressure recorded as 180/110 mm. mercury. The patient was admitted to the hospital for investigation.

During the course of study, the chest x-ray revealed hilar lung lesions suggestive of Boeck's sarcoid. In addition, the persistent hypertension was noted and the patient was then transferred to Brooke Army Hospital. Past history and family history were noncontributory.

At the time of admission to Brooke Army Hospital, examination revealed a well-developed, well-nourished, apprehensive white male in no acute distress. Examination of the head and neck was negative. Funduscopic examination revealed a grade 1 arteriolar constriction. The lungs were clear to auscultation and percussion. There was suggestion of mediastinal widening in the second, third and fourth interspaces. The heart was enlarged to percussion, with the left border being at the left anterior axillary line in the sixth interspace. There was a grade 1 systolic murmur which faded toward the base. Pulse was 90, of good quality and regular. Blood pressure: Right arm 170/92; left arm 168/100; left leg 220/120. Abdomen was scaphoid in type and no tenderness or masses were noted. A loud bruit was heard in the left lumbar area below the left costal margin. The genitalia were normal. Neurological examination revealed no abnormalities.

Laboratory and x-ray studies: Urinalysis and blood studies were within nor-

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mal limits. Serology was negative; urea clearance was normal. Blood urea nitrogen was 18.5 mg. per cent. A chest x-ray taken shortly after admission revealed a cardiac silhouette grossly enlarged with hypertrophy or dilatation of the left ventricle (fig. 1, *A*). The CT ratio was 18/31; prominence of the pulmonary conus was also noted. There were bilateral enlargements of the hilar glands consistent with the diagnosis of Boeck's sarcoid. An electrocardiogram on September 20, 1950 revealed a left ventricular preponderance. An excretory urogram revealed a normal right kidney and ureter; on the left side the collecting system could not be well demarcated, although there appeared to be elongation of the calyces of the left kidney. Scalenus anticus lymph node biopsy was performed and this revealed only chronic lymphadenitis. Bone marrow studies revealed normal granulopoiesis, erythropoiesis and thrombopoiesis. The patient was then referred to the Urology Clinic by the Medical Service. On September 25, 1950, retrograde pyelography was performed. This again demonstrated a normal right kidney. The left collecting system had a bizarre appearance with elongation and dilatation of the superior calyx (fig. 1, *B*).

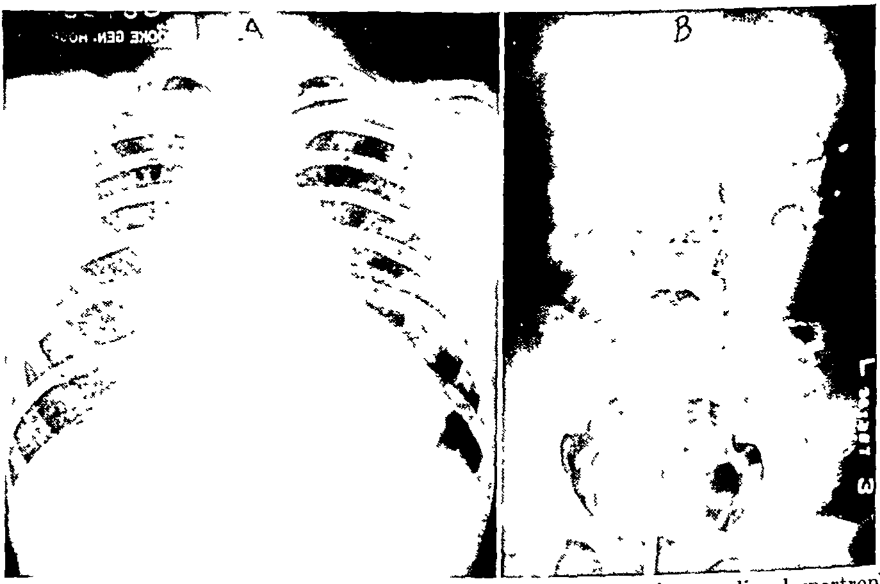

FIG. 1 *A*, roentgenogram of chest on admission demonstrating cardiac hypertrophy and enlarged hilar nodes *B*, retrograde pyelogram showing space-occupying lesion of left kidney.

The clinical impression was that this patient had a space-occupying lesion of the left kidney producing an arteriovenous fistula, accounting for the loud bruit heard over the left renal area. The patient was then transferred to the Urology Service.

On September 26, 1950, a left nephrectomy was performed through the usual left lumbar incision. At operation, it was noted that the kidney was replaced by a tumor mass occupying over two-thirds of the kidney tissue. There were multiple engorged large veins in the perirenal fat As the kidney was freed, it was noted that the renal vein was markedly enlarged. After the application of pedicle clamps, the elevated blood pressure stabilized at a new low level of 100/60. Following removal of the kidney, it was noted that there was extension of tumor tissue into the enlarged renal vein; however, there was no extension of tissue beyond the point of excision.

Pathology report: Gross: The specimen is labeled "left kidney" and weighs 550 gm. It measures 15 by 8 by 8 cm. Perinephritic fat remains attached to the capsule. The external surface of the kidney is irregular, lobulated, and many small hard nodules are palpated on the surface. The renal capsule is markedly adherent throughout. It can only be stripped from a small area at the lower pole. A fistulous connection can be demonstrated between the renal artery and renal vein by passing a probe from one vessel into the other. (fig. 2). The renal vein is grossly filled with tumor mass. On cross section, the entire renal mass appears to be filled with tumor tissue except the extreme lower pole. At the superior pole, there is a large tumor mass measuring 5 cm. in diameter which has a necrotic area near its middle measuring 2 cm. in diameter. Representative sections were taken from all portions of the kidney.

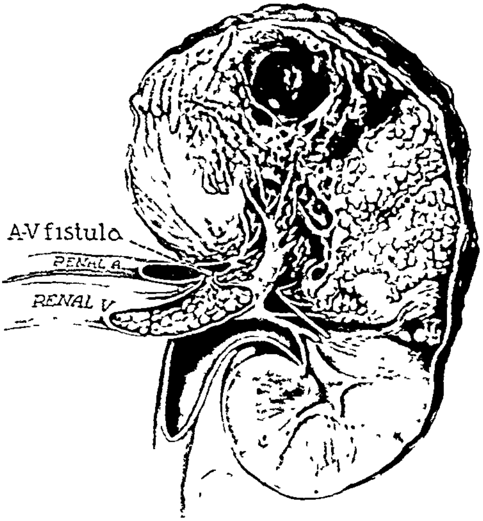

FIG. 2. Artist's conception of pathological specimen demonstrating arteriovenous fistula.

Microscopic examination: Sections taken through the kidney tumor show it to be composed of a papillary type of growth forming numerous projections as well as numerous acini. The individual cells generally are rather large and show clear to slightly granular cytoplasm. Their nuclei are round to oval and generally contain finely granular chromatin. Many of them contain rather prominent nucleoli. Both the cells and the nuclei vary considerably in size and shape. Mitotic figures are moderately common. In most areas the tumor assumes a papillary or acinous-like arrangement; however, in some areas the cells grow in rather broad sheets. Considerable areas of the tumor show quite marked necrosis and degenerative change. The tumor actively invades the surrounding kidney substance which is also compressed by its growth. There is a very extensive growth around the hilus of the kidney and small fragments of tumor tissue are seen in small arteries and veins. The tumor tissue which was grossly seen in the renal vein is not demonstrated in these sections. A portion of the kidney taken from the uninvolved area near the lower pole shows nothing unusual except for some postoperative degenerative change. This is an actively growing malignant adenocarcinoma of the kidney with most of the cells of the clear cell or hypernephroma type. Diagnoses: Kidney, adenocarcinoma; renal vein, adenocarcinoma, secondary; renal artery and vein, arteriovenous fistula.

Postoperatively the patient convalesced well. His blood pressure became stabilized at 140/90 mm. of mercury. The bruit was no longer heard postoperatively. By October 12, 1950 the patient was considered to be sufficiently recovered to be sent on a convalescent leave. On his return, a review of the chest x-rays was made by the chest consultant and the consensus of opinion was that despite the adenocarcinoma of the kidney, the lesion was still considered to be Boeck's sarcoid. A followup chest x-ray on January 4, 1951 showed no change in the hilar nodes and a reduction in the size of the cardiac shadow with the CT ratio being 14.5/31 cm. The patient was discharged to full military duty on January 19, 1951.

DISCUSSION

Arteriovenous fistula of the renal vessels is a rare entity. Varela reported the first case in 1928. His patient was a 28-year old male with severe cardiac decompensation and mild hypertension (160/80). The origin of the lesion was suspected clinically by the presence of a murmur in the right lumbar area and proven at autopsy. The fistula formation was believed due to erosion from a congenital aneurysm of the renal artery. Rieder's case similarly had severe cardiac decompensation but with definite hypertension (220/120). A thrill and bruit heard in the right lumbar area aroused suspicion of the nature of the lesion preoperatively. A congenital aneurysm was believed to cause this lesion; however, this patient did have a history of right flank injury in 1940. Nephrectomy cured this patient. The third case, reported by Pearse and MacMillan in 1947, showed only gross hematuria clinically. There was no cardiac decompensation, no hypertension, and no bruit was noted preoperatively. On examination of the surgical specimen, an arterial and a venous aneurysm were found with a fistulous communication between them. The authors believed these to be congenital aneurysms with erosion forming the fistula. Our case presented hypertension and a loud bruit over the left kidney, leading to the preoperative suspicion of arteriovenous fistula. In the three cases previously reported, the cause of the fistula-formation was believed due to an aneurysm. It is surprising that no other reports of this lesion associated with renal neoplasm have been recorded. Varela does mention a case (Fircks) in which an aneurysm of the renal artery and hypernephroma were associated with a severe hypertension, cured by nephrectomy. The Armed Forces

Institute of Pathology has no cases of arteriovenous fistula of the renal vessels on file.

The effects of arteriovenous fistula on the heart and blood vessels have been amply discussed by Reid. The unique position held by arteriovenous fistula of the renal vessels in being the only such communication causing hypertension has been well described by Rieder, Hollingsworth, Lasher and Glenn. We believe that our case demonstrates the salient features of this lesion and is unusual in being associated with an adenocarcinoma of the kidney and Boeck's sarcoid. We regret that an aortogram was not made.

SUMMARY

The fourth case of arteriovenous fistula of the renal vessels is reported; this is the first case recorded in which the etiology was adenocarcinoma of the kidney.

A brief review of the literature on this subject is presented.

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TABLE 1. *Tabulation of cases*

AVERAGE AGE	SEX	SIDE OF OPERATION	SYMPTOMS	INFECTION	OPERATION	RESECTION OF PELVIS	CALIBER OF SPLINT	AVERAGE DAYS OF SPLINTING	FOLLOW UP STUDIES			
									Symptoms	Infection	*Results*	Months follow up
31	M 1 F 15	R 12 L 6	94%	50%	Foley 13 Davis 4 Mikulicz 1	Yes 5 No 13	2 none 11 8F 4 10F 1 12F	25	None	None	Fair 2 Excellent 16	17½

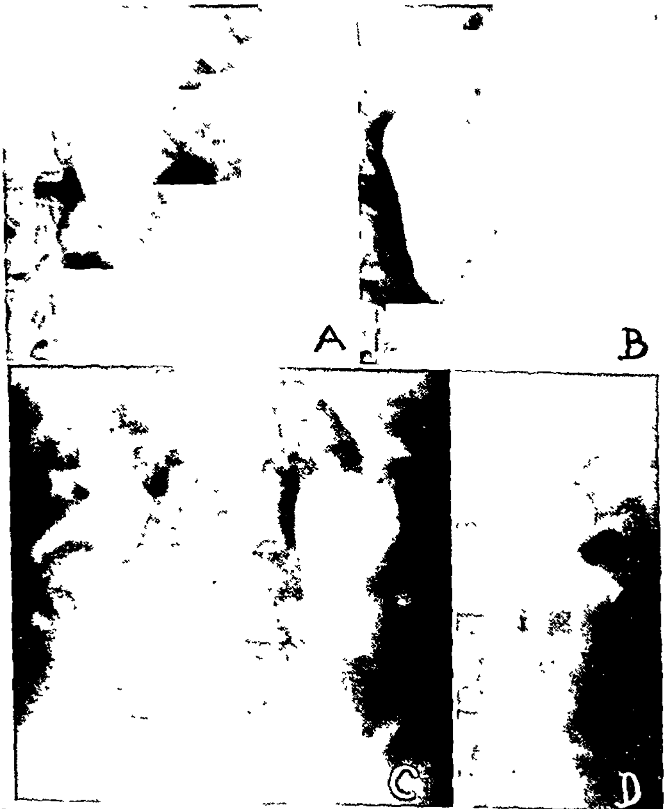

FIG. 1. Case 1. *A*, left ureteropyelogram. Hydronephrosis grade 2; seven small calculi in pelvis; Proximal ureter hairline with elevated exit from pelvis. *B*, film taken 60 minutes following *A* disclosed marked failure of evacuation. *C*, excretory urogram 40 minutes following injection of diodrast and 14 months after pyeloplasty. Patient 7 months pregnant. Excellent funnel of proximal ureter evacuating pelvis at most dependent portion; usual bilateral dilatation of both pelves associated with pregnancy. *D*, left ureteropyelogram 26 months from time of operation, 10 months post partum. Calyces assuming delicate contour; pelvis reduced in size; proximal ureter dependent and funnelled.

in 18 days. *Incrustations* were present. No leakage occurred through the fistula. The urine was free of infection 47 days postoperative, 29 days following removal

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EXPERIENCES WITH PYELOPLASTY

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Up until 1948 we had looked upon pyeloplasty with a jaundiced eye. We harbored this pessimism because, even though papers were presented, it was rumored among urologists that ultimate results were discouraging. We decided that even though as high as 50 per cent failure might be encountered, in the name of conservation of renal tissue, we would be justified in attempting this operation.

The surgeon needs the reassurance of experience in elective cases in order to confidently face a particularly critical situation: 1) obstruction in a solitary kidney; 2) bilateral obstruction; 3) obstructions unexpectly encountered at operation.

We wish to present pictorially our experiences in 18 pyeloplasties on 16 patients.* These are consecutive cases, good and bad, performed since 1948. The cases are analyzed in table 1. We will offer a few practical suggestions concerned with the diagnosis, technique of operation and after care which we have learned from our experiences.

CASE REPORTS

Case 1. A white woman aged 28 was seen in February 1948. She had no symptoms. Pyuria was discovered during a routine physical. Examination was negative. Investigation revealed hydronephrosis, left, with seven small calculi in the pelvis. The right upper urinary tract was normal. February 18, 1948, Foley Y plasty; Cummings splint; removal of calculi; nephropexy. The splint was removed in 20 days; the tube was incrusted. No leakage occurred through the fistula. The urine was free from infection 29 days after removal of the splint.

Figure 1, *A* demonstrates the advantage of an ureteropyelogram in contrast to a pyelo-ureterogram as a means of demonstrating the ureteropelvic junction.

The excretory urogram made at 7 months of pregnancy provides an exaggerated view of the ureteropelvic anastomosis.

Case 2. A white woman aged 24 was seen in February 1948. She had pain in the left upper quadrant and left sacro-iliac region, chills, high fever, urinary frequency and burning. She had had a miscarriage at 6 months in 1945; at 4 months in 1947; surgical abortion for hypertension and pyelonephritis in January 1948. The left kidney was palpable and tender. The urine was infected with Aerogenes. She had left hydronephrosis grade 3, and congenital absence of the right kidney. Operation, February 24, 1948: The kidney was large and the pelvis extrarenal, the size of a baseball. Dense adhesions were present between the ureter and pelvis, and high insertion and stricture of the ureter were found. Foley Y plasty (McIver tube) and nephropexy were done. The splint was removed

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Read at annual meeting, Southeastern Section, American Urological Association, Memphis, Tenn., March 10, 1951.

* The 18 case reports were presented in detail at the meeting in Memphis. At the request of the editors, only 5 cases will be presented.

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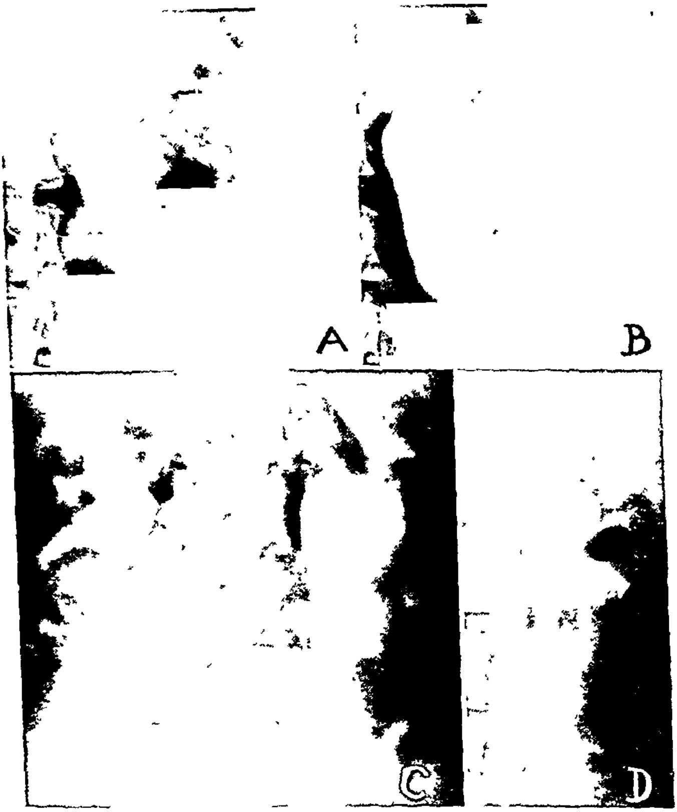

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in 18 days. Incrustations were present. No leakage occurred through the fistula. The urine was free of infection 47 days postoperative, 29 days following removal of splint. The patient was asymptomatic, free of pain, had normal urination and was gaining in weight. The presence of ureteropelvic obstruction in a solitary kidney demanded a successful result.

Case 3. A white woman aged 42 years was seen in March 1949. She complained of right flank pain for 15 years, and hypertension of unknown duration. Culture of the urine was positive for Aerogenes. The left pyelogram was normal. On March 22, 1949, Foley Y plasty was done. Inelastic constriction of the ureteropelvic junction was present. The pelvis was resected. A polyethylene 8F tube was used for a splint. Nephrostomy and Deming and Kelly nephropexy were done. Following operation, streptomycin and sulfa drugs failed to control the temperature which varied between 102 and 106F for 5 days. (Other drugs were not available.) The splint was removed in 6 weeks; no incrustations were

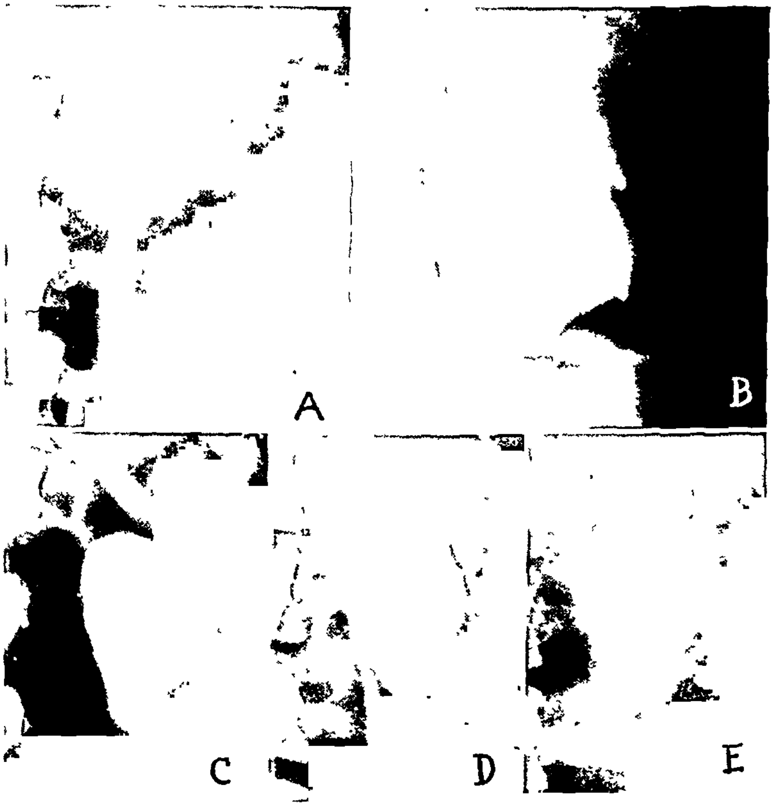


FIG. 2 Case 2. *A*, left ureteropyelogram. Hydronephrosis grade 3; calyces blunted; large capacity of pelvis with convex borders; stricture of ureter at most proximal portion; lumen hairline; ureteropelvic junction elevated; congenital absence of right kidney. *B*, upright exposure disclosing marked ptosis. *C*, evacuation film 30 minutes following retrograde injection exhibiting retention. *D*, left ureteropyelogram 13 months following operation. Calyces more delicate; some reduction in capacity of pelvis; contour of borders of pelvis slightly less convex; ureteropelvic junction not ideal; failure to obtain funnel and exit of ureter above most dependent portion of pelvis; proximal ureter relatively narrow. Results suggest failure of sutures to hold. Also the limbs of the Y were not designed sufficiently long. *E*, evacuation film 15 minutes following injection of skiodan through Braasch bulb in lower ureter. Moderate retention remains.

present. The nephrostomy tube was removed the seventh week. The fistula closed without leakage. Urine cultures were negative in 2 months. The patient was asymptomatic. The improved postoperative pyelogram (fig. 3, *C*) may partially be attributed to the resection of the pelvis. Figure 3, *B* gives a discouraging and false impression of the results of the operation because only 2 months had elapsed. Repair was in progress.

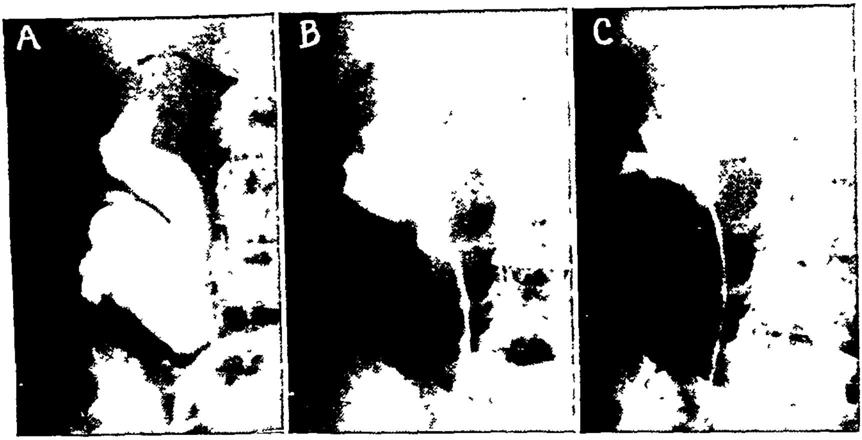


FIG. 3. Case 3. *A*, retrograde pyelogram. Large extrarenal pelvis; redundant ureter; parenchyma preserved. *B*, pyelogram 2 months postoperative demonstrates discouraging appearance spuriously. *C*, pyelogram 9 months postoperative. Calyces remarkably improved.

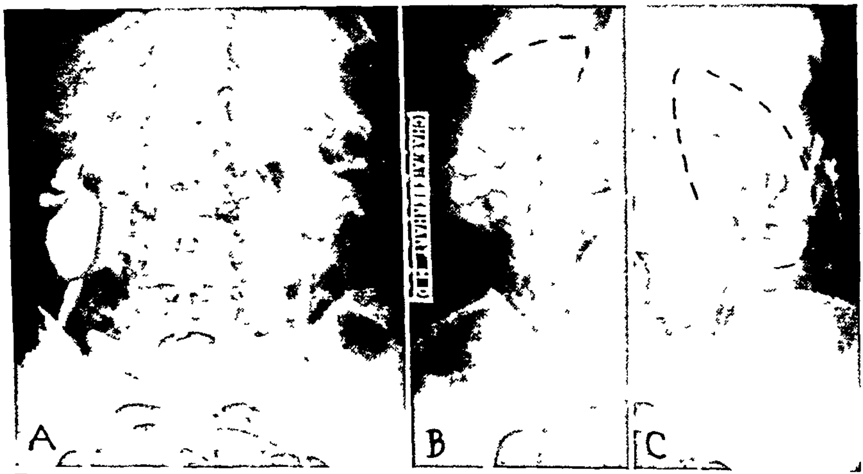


FIG. 4. Case 4. *A*, retrograde pyelogram Bilateral ureteropelvic obstruction; hydronephrosis; bilateral third degree nephroptosis also present. Ten minute film, 50 per cent residual, bilateral. *B*, right ureteropyelogram 1 year after operation. Ten minute emptying film, no residual. Mild regression of hydronephrosis. *C*, left ureteropyelogram 5 months after operation. Ten minute emptying film, no residual.

Case 4. A woman aged 38 years was seen May 28, 1949. She complained of bilateral lumbar pain of long standing. The urine was not infected. On June 16, 1949, right Foley Y plasty, and resection of pelvis. Ureteropelvic obstruction was present. A 8F urethral catheter was used for a splint. Nephrostomy and Kelly nephropexy were performed. The postoperative course was stormy. At operation, a button-on catheter collapsed when inadvertently pulled into the lower minor calyx, the pelvis no longer large enough to harbor it. Likewise the nephrostomy tube was not irrigated before closure of the wound; consequently, it did not drain and was removed on the fifth day. An ileus developed on the seventh day. On the tenth day the lower angle of the wound was reopened to allow the escape of a large amount of infected urine from the lower pole of the kidney. The splint was removed on the fourteenth day; no encrustation had occurred. The fistula was closed without leakage. Culture of the urine yielded staphylococci, but the infection cleared with the use of sulfadiazine

August 1, 1950, left Foley Y plasty and resection of the pelvis were done. No demonstrable ureteropelvic obstruction was found. No splint or nephrostomy drain was used. A Deming nephropexy was done. Urine leaked from the wound after the fifth day. On the eighth day the urine contained numerous pus cells but no micro-organisms, and became clear microscopically on the twenty-fourth day. Bilateral phenolsulfonphthalein excretion was normal the fifth month. The patient gained weight for the first time in her life, became asymptomatic and remarkably improved. Because of the presence of bilateral ureteropelvic obstruction, the life of this patient depended on a successful result. (Under certain conditions splendid results can be obtained without the use of splints or a nephrostomy.)

Case 5. A woman aged 21 was seen in August 1950. She complained of right renal pain. For 1 week she had had chills, fever, symptoms of bladder infection, anorexia, and acute tenderness in the right upper quadrant and loin. Right hydronephrosis grade 1, infected urine and ureteropelvic obstruction were present. The left kidney was negative. October 3, 1950, Foley Y plasty and nephropexy were performed. The splint, a Cummings 8F, was removed in 21 days; no incrustation had occurred. No leakage occurred from the fistula. The patient had obtained complete relief. The culture of the urine was reported sterile 2 weeks after removal of the splint. The patient's lifetime digestive disturbances were completely alleviated, and severe facial acne of many years' duration spontaneously improved. The limbs of the Y were made as adequate as the anatomy would permit. This detail was responsible for the splendid result.

PRACTICAL SUGGESTION FOR IMPROVED CARE

Diagnosis. Cahill has emphasized that retrograde pyelography on a hydronephrotic kidney is fraught with the danger of implanting infection. He operates solely on the evidence of excretory urography. This may be highly desirable. By meticulous attention to the details of sterilization and timely use of the newer drugs, retrograde pyelography in our hands has not induced infection. We are convinced that the ideal preoperative study consists of excretory urography, followed by uretero-pyelography using a Braasch bulb to occlude the ureterovesical orifice on the affected side. Foley has mentioned the maneuver and we wish to re-emphasize the efficiency of this technique. An excellent pictorial demonstration of the proximal ureter and ureteropelvic junction is produced. By this method more details of the actual type and degree of obstruction with attendant changes are more often visualized than actually seen at operation. One is often impressed with the minor degrees of pathological changes seen at surgical exposure in comparison with the degree of obstruction as depicted by the pyelogram. In 72 per cent of the cases of this series, the pyelogram delineated the obstruction more convincingly than did actual surgery. If the doctor is not mentally convinced of the obstructing picture prior to surgery, then he may desist from following through with the plastic procedure when the kidney is exposed. The pyelogram alone should justify the necessity of operation.

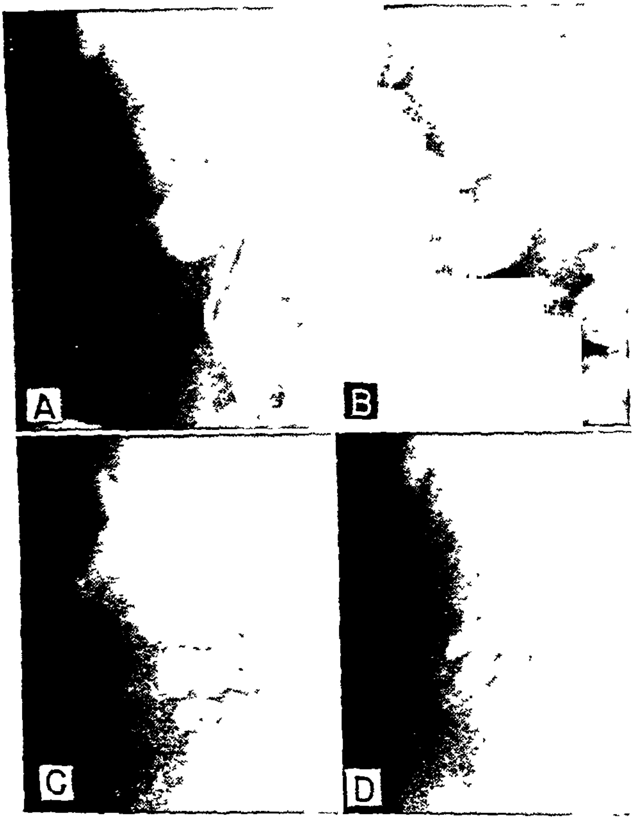


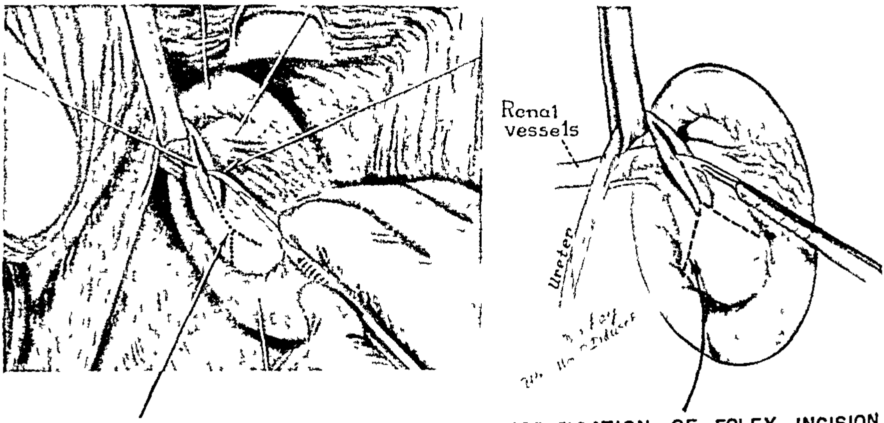
FIG. 5. Case 5. *A*, right ureteropyelogram. Hydronephrosis grade 1. High insertion of ureter. ureteropelvic adhesions, half-inch stricture of proximal ureter. *B*, evacuation film showing retention at 15 minutes. *C*, right pyelogram 3 months after plastic operation. Deformity of ureteropelvic junction completely corrected; hydronephrosis receding. *D*, emptying film. 5 minutes, revealing excellent drainage.

OPERATIVE TECHNIQUE

The incision in pelvis. The incision into the ureter and pelvis must not be puny. Too much emphasis cannot be placed on the advisability of making the limbs of the Y in the Foley operation as long as design will permit. In our earlier cases we were guided by the interpretation of the artist in the original article of Dr. Foley (fig. 6). It became apparent that the small V resulting from this type of incision did not provide a sufficiently long funnel when completed. We were impressed with the greater adequacy of the ureteropelvic junction when the incision was carried along the pelvic wall as far as the parenchyma (fig. 6).

Nephropexy. Nephropexy is considered an important part in the ultimate success of the plastic procedure. The fixation of the kidney maintains the relationship of the splints in the freshly sutured pelvis when other body positions are resumed.

Splinting. Those who have written on this subject differ as to the duration of maintenance of the splint in the ureter. Our experience dictates that an average period of 3 weeks permits sufficient time for molding and healing. A longer stay encourages calcium deposition and maintenance of infection thereby placing in jeopardy the integrity of the plastic repair. We concur with Dr. Davis that 6 weeks is preferable in the intubation operation. In one of our cases (No. 10) a child of 9 years, the splint was accidently removed on the eleventh day. It became necessary to re-expose the kidney in order to replace the splint accurately. At operation one could observe that the incision in the ureter was quite evident and the edges had not coalesced.



FOLEY ORIGINAL INCISION MODIFICATION OF FOLEY INCISION

Fig 6

More recently no splint was used in 2 cases. The results were encouraging. In 1943 Deming advocated dispensing with splints and stated that for the preceding 18 years he had not employed any means of drainage in cases which were uninfected.

The type of material used in splinting is of some importance. We have found an ordinary soft urethral catheter to be equally as efficient as the more complicated apparatus; besides, the urethral catheter is always available and less expensive. In 1 case a polyethylene splint was used, but it was found to be too rigid and unyielding and caused an exaggerated bowing of the ureter.

The combination of separate nephrostomy tube and urethral catheter is more advantageous than the combined variety of nephrostomy with splint. Thus, the splint may be removed separately, the nephrostomy maintained as long as desired. This becomes especially important when severe infection is present. Through the nephrostomy tube pyelography may be easily performed obviating the necessity of cystoscopy. This proves a decided advantage in children avoiding anesthesia and hospitalization.

Resection of pelvis. We are divided in our opinion about the advisability of resecting a redundant renal pelvis. An improvement in the delineation of the ureteropelvic junction and calyces from the absence of an overshadowing distended pelvis may be obtained in the postoperative pyelogram. However, resection of the pelvis does not seem to be necessary for the success of the operation.

POSTOPERATIVE CARE

Infection. In cases where free flow of urine has been established, infection should spontaneously disappear without drugs within a month from the time of the removal of all splinting materials. This is likewise true in individuals who have large pelves with varying amounts of residual urine.

If it can be avoided, we never disconnect the joints of the tubing. We do not irrigate the renal pelvis through the nephrostomy tube for fear of introducing infection.

A specimen may be obtained for urine culture at any time simply by aspirating the nephrostomy tubing through its wall by a hypodermic needle.

Acidification of urine. It is conceded that splints induce infection. Infections encourage deposition of calcium salts on splinting materials. Thus drainage tubes become occluded. We attempt to combat salt deposit by acid ash diet, and acidifying agent and appropriate chemotherapy.

Ambulation. Some may veer away from early ambulation in patients undergoing nephropexy. We have had all patients in this series out of bed within 24 hours without ill effects.

Pyelography. Every surgeon contains sufficient vanity to demand satisfaction of the curiosity to appraise the results of operation by pyelography. We were not immune. In the earlier cases post-surgical pyelograms were performed a month after operation. One cannot obtain an accurate picture of the results so soon after surgery. At this time there is edema and infiltration of tissues associated with the process of repair. The pyelogram will reflect this process of healing and the surgeon may experience keen disappointment that the operation was unsuccessful. Accordingly, and in spite of the personal anxiety, one should not expect a true picture until a period of at least 3 months has elapsed. By this time the healing process has subsided. The picture at 3 months will provide an excellent trend of the ultimate future result. Subsequent to 3 months none or only gradual improvement may occur. If the pyelogram disclosed a desirable picture then one may feel confident that this result will improve with time. While long range postoperative pyelographic studies are interesting, and make for better records and provide teaching material, they are not influential in formulating prognosis.

EVALUATION OF RESULTS

To place an arithmetic value on our results by any stereotyped criteria would seem inaccurate and misleading. It was only during the preparation of this paper that the cause of our mistrust for pyeloplasty occurred to us. This doubt was due to our urologic mindedness in judging results on the basis of a pyelogram. The postoperative pyelogram presents tangible evidence of a final result and is stressed in all presentations. It is often disappointing in its appearance, as is true in a number of our cases. Actually, the pyelogram, while pictorial and dramatic, is not the entire story and often of minor importance. Final evaluation must be made on a less spectacular and less tangible basis namely: improved physiology, absence of infection and clinical improvement. We believe that an excellent physiological result has been obtained in each of our cases. In not one case did the infection persist in the urine. In those patients who had preoperative urological symptoms, a remarkable and gratifying improvement has occurred in the general health far exceeding that which one would expect solely from relief of urological symptoms. To a degree this is also true of those patients who were preoperatively asymptomatic. This desirable improvement has been obtained in all except one instance (case 8). Paradoxically, the pyelogram in this patient exhibits one of our most impressive results. We believe her symptoms, although local, are originating outside the urinary tract, and are of functional origin.

Our personal experiences maintain our enthusiasm for this procedure. Secondary nephrectomy has thus far not been required. We readily admit that these cases have been followed over a short time, averaging 17½ months. However, as previously stated, one may form a fairly accurate opinion of ultimate long range results by the clinical appraisal within 3 to 6 months following surgery. There have been no fatalities and morbidity has been minor and inconsequential.

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URETERAL MANAGEMENT FOLLOWING REMOVAL OF THE BLADDER AND LOWER BOWEL FOR CARCINOMA

LOWRAIN E. McCREA

Diversion of the urinary stream by transplantation of the ureters into the skin is a surgical procedure of considered excellence. Due to its merit as a surgical procedure, the possibilities of aid to some individuals are believed to be greater than those achieved by any other surgical procedure for the management of the ureters when pelvic evisceration is indicated.

Problems frequently confront a surgeon as to the proper mode of management of the ureters in any consideration of surgical treatment of the carcinoma of the bowel with extension to or involvement of the urinary bladder. This is particularly true when a Miles resection is contemplated. Excision of the lower bowel, as is done in a Miles resection, precludes any possibility of ureterosigmoidostomy. The transplantation of the ureters into the bowel alone, with the creation of a wet colostomy, is not desirable. The implantation of the ureters into a freed segment of the bowel, having an external communication on the skin of the abdomen, has been advocated by some surgeons. Such a surgical procedure has yet to be clinically proven. It is believed that infection and the risk of pyelonephritis would be great with this latter procedure. Cystotomy would divert the urinary stream but would not eliminate the carcinomatous invasion of the bladder nor relieve compression of the lower ureters. Cutaneous ureterostomy, with associated colostomy done simultaneously with resection of the bowel and bladder, possibly offers the greatest potentialities of relief and the greatest possibility of comfort to those individuals requiring such extensive surgery. However, such surgery is not warranted if the gross neoplasm cannot be removed or if metastasis can be demonstrated.

Papin is credited with having performed the first cutaneous ureterostomy and cystectomy in 1913. The transplantation of the ureters into the skin was first proposed by Gignon in 1856 but the operation was first performed by Simon in 1869 who accidentally cut a ureter during an ovarian operation. Laurenze, of Rome, is credited with having performed the first deliberate cutaneous transplantation in 1856, but the details of the operation, the clinical course and results are not available. In 1889, Le Dentu successfully performed the operation and is accredited with having done the first deliberate cutaneous ureterostomy. The ureter was placed in the loin by the pioneer surgeons. It was not until 1921 that Legueu and Papin presented their technique for transplantation of the ureters into the iliac region of the abdomen. In America, Beer, in 1929, was the first to report the successful application of bilateral cutaneous ureterostomy and total cystectomy with implantation of the ureters through a stab incision in the groin. Since that time many surgeons, realizing the value of the procedure, have repeatedly used cutaneous ureterostomy for many and varied conditions necessitating

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diversion of the urinary stream. It is only within recent years that pelvic exenteration has been used in the radical treatment of extensive malignancy. One of the major problems confronting the surgeon was the management of the ureters.

It is believed that cutaneous ureterostomy has never been well received by American surgeons. Uretero-enterostomy has received more attention and has gained much more popularity than cutaneous ureterostomy. But, with elimination of the sigmoid, such a procedure is out of the question. The indications for the two procedures are somewhat varied. No attempt will be made here to compare the two procedures either from a technical standpoint or the standpoint of indications.

The end results of cutaneous ureterostomy are possibly more satisfactory than those following other suggested types of surgical management of the ureters. The cutaneous implantation of the ureters is done at the time the colostomy is made and the pelvic evisceration is done. The entire operation is a single stage procedure. Cutaneous ureterostomy is a relatively simple procedure and is rapidly performed when the abdomen is opened. The operation does not require a specialized preoperative or postoperative regimen. The operation insures adequate postoperative urinary drainage. Should infection exist before operation, or occur following transplantation, free, adequate drainage is assured and the control of such infections is usually simple. It is generally conceded that indwelling ureteral catheters offer the greatest ease to these patients postoperatively. Appliances are available for the collection of the urine from the ureters without the use of catheters, but the use of properly placed indwelling ureteral catheters is generally conceded to be more advisable. The patient and/or his family may be easily trained in the care and management of indwelling ureteral catheters and the collecting apparatus.

The main surgical disadvantage to this procedure is the occurrence of sloughing and retraction of the terminal end of the ureter. It is considered that sloughing occurs as the result of interference with the blood supply by too extensive freeing of the ureter of the peri-ureteral tissue which contains its nutrient blood supply. Retraction of the terminal end of the ureters is usually due to tension on the ureter caused by its not being properly freed at the time of operation. The ureter, at the time of surgery, should project from its new aperture without any tendency to retract before the anchoring suture is applied. The greatest disadvantage to the patient of cutaneous ureterostomy is the necessity of wearing an appliance for the collection of urine. This appliance, together with a colostomy bag, offers its problems. In spite of these appliances, patients adapt themselves readily to their care and management.

The ideal surgical team to perform such extensive surgery consists of a colonic surgeon and a urologist. The colonic surgeon does the bowel phase and the urologist does the urinary tract phase of the procedure. The procedure of cutaneous ureterostomy varies considerably from that of extraperitoneal cutaneous implantation when done without evisceration. It is suggested that before operation the desired point of exit of the ureteral stoma be adequately marked. It is considered that the better location of these points of exit is above the level of the iliac crest about 8 to 10 cm. medially to the anterior iliac spine. These points of exit may be marked with gentian violet which will withstand, but not interfere with, the usual preoperative skin preparation. The technique is illustrated in figure 1. A left paramedian incision, beginning at the level of the symphysis extending upward above the level of the umbilicus, is advised. Following exploration of the abdomen the small intestine is walled off by moist gauze pack. The bowel is mobilized. When cystectomy is to be done, no attempt is made to free the rectum from the posterior wall of the bladder.

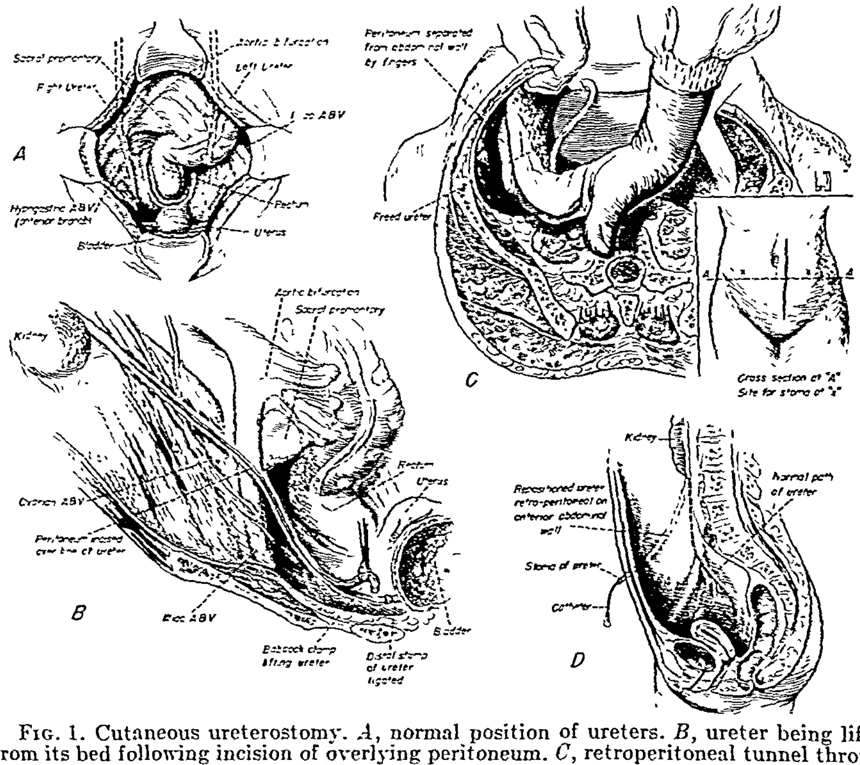

FIG. 1. Cutaneous ureterostomy. *A*, normal position of ureters. *B*, ureter being lifted from its bed following incision of overlying peritoneum. *C*, retroperitoneal tunnel through which ureter will pass to its new location. *D*, position of ureter following transplantation in contrast to position of normally placed ureter.

The ureters, individually, are located. The peritoneum is incised at the level of the promontory of the sacrum and the ureter is grasped by visceral forceps. The incision of the peritoneum is carried downward along the course of the ureter to the bladder. The ureter is dissected from its bed to its juncture with the bladder or to a point sufficiently above any carcinomatous envelopment. The tissue immediately surrounding the ureter should be permitted to remain in situ. It is within this tissue that the nutrient blood supply to the ureter is located. The ureter is clamped. Ligation is made below the clamp and the ureter is severed immediately above the clamp. The ureter is immediately brought out of the wound and a catheter instituted to the renal pelvis. The catheter of choice is of Latex, whistle tip in type. The largest size which can be accommodated by the ureter should be used. Freeing of the ureter may then be continued upward for any desired length to permit its upward and lateral displacement on the abdominal wall. Utilizing the incision in the peritoneum on each side, a tunnel is made by blunt dissection to a point about 8 cm. medial to the anterosuperior spine of the ileum. This point has previously been marked by gentian violet. At this point a stab wound is made through the abdominal wall. The ureter is brought through the tunnel in the retroperitoneal space and the distal end is brought out of the stab wound. The end of the ureter should protrude, without tension, through the stab wound at least 2½ cm. To prevent unavoidable retraction by motion in bed, the ureter is anchored by two silk sutures. The sutures are placed through the adventitious tissue surrounding the ureter and the abdominal fascia. The catheters remain in situ. The urine is diverted away from the wound by the ureteral catheters while the remaining portion of the abdominal phase of the operation is completed.

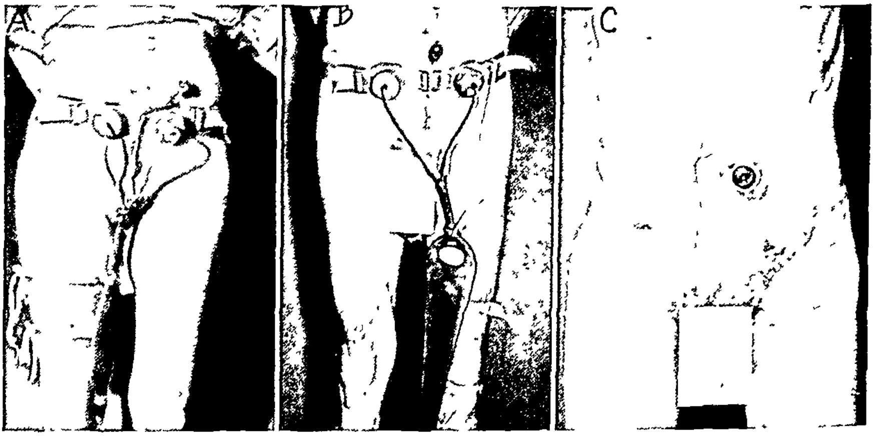

FIG. 2. *A*, position of ureteral stoma in relationship to previously placed colostomy opening. Note level of ureteral cups and catheters. *B*, proper position for cups and catheters. It will be noted that colostomy is very low having been done before cutaneous ureterostomy became necessary. *C*, improperly placed ureteral stoma in relationship to iliac crest. It is difficult to maintain collecting apparatus in such low position of stoma.

It is suggested that the anterior branch of the internal iliac or hypogastric artery be ligated at such a point that the posterior branch of the artery is not included in the ligature. The ligation of this artery will prevent considerable blood loss during the procedure of the cystectomy and resection of the bowel. The rectum and that portion of the sigmoid to be removed are then freed by blunt and sharp dissection liberating the root of the sigmoid to the tip of the coccyx. In women, removal of the uterus must be done. The peritoneum is then incised anteriorly over the bladder. The bladder is liberated by blunt dissection anteriorly and laterally. By retracting the bladder cephalad, the hand may be swept anteriorly and downward until the ligamentous attachments to the symphysis are reached. Blunt dissection is continued downward until the base of the bladder is liberated and the prostate is clearly defined. No attempt is made to separate the prostate from the rectum. The bladder, after liberation, is retracted to form a part of the large mass of diseased rectum, sigmoid colon, lymphatic and other tissue which are removed en masse from below. The sigmoid colon is divided between clamps in its upper third, the proximal segment to be utilized as a permanent colostomy. The abdomen is closed after the colostomy has been placed in the midline above the umbilicus. The perineal phase is now done. With the patient in the lithotomy position, the perineum is entered through a shield shaped incision extending from a point overlying the posterior urethral-laterally to the ischial tuberosities. The incision is then extended medially to the tip of the coccyx. The ischio-rectal space on either side is cleared of fatty tissue exposing the levator muscles. Anteriorly the posterior urethra is freed of muscle and adventitious tissue. Posteriorly, the tip of the coccyx is reached. Laterally the levators are separated from their origins. The pelvic cavity is entered. The urethra is freed, ligated and divided immediately distal to the prostate. The prostate is then freed by blunt dissection. Anteriorly the ligamentous attachments between the bladder and the symphysis pubis are divided. The entire pelvic mass of diseased and potentially diseased structures are delivered en bloc through the perineum.

The postoperative care of the ureter and ureteral stoma is important (fig. 2). Improper care of the ureteral stoma may lead to retraction of the ureter with possible peri-ureteral extravasation, angulation of the ureter or stricture of the ureter. It is imperative that the ureter lie in its new position without tension. The catheter originally instituted should be of the largest diameter which can be accommodated by the individual ureter. It has been suggested that a Foley (5 cc balloon) catheter be used. However, it is possibly more difficult for the patient to care for such a catheter. Immediately following surgery the catheters are permitted to drain each into a separate reservoir. When the patient is permitted out of bed, the belt appliance is applied. The belt is so constructed that it maintains the correct position of the catheters as well as providing attachment of the leg urinal.

The mode of management of the ureters in complete pelvic exenteration has been presented. It has been surprising and very gratifying to note the rapidity of convalescence of those patients subjected to cutaneous ureterostomy and pelvic evisceration. It is believed that the procedure offers the greatest possibility of rehabilitation to those patients upon whom such extensive surgery is indicated.

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IDIOPATHIC SEGMENTAL URETERAL ECTASIA IN A CONGENITAL SOLITARY KIDNEY

JOSEPH A. LAZARUS AND MARIO W. RICCI

In 1896 Saintu reported the first example of congenital idiopathic ureteral dilatation in a 7½ month old fetus, with hydronephrosis, relaxed atonic ureteric orifices. There was no evidence of infravesical obstruction. Since then several reports appeared in the literature of urology pertaining to the condition in newborn infants and children. Caulk, in 1923, was the first to use the term "megalo-ureter" in describing the condition of a patient with an enormously dilated ureter and a normal renal pelvis, probably caused by a primary anatomic defect in the ureteral wall.

A careful review of the literature failed to reveal many examples of ureteral ectasia where the defect was limited to a single segment of the ureteral lumen without evidence of hydronephrosis. Morris (*Surgical Diseases of the Kidney and Ureter*) contributes an illustration of a saccular dilatation of the ureter directly below, but not involving, the renal pelvis (Guy's Hospital Museum, No. 1704).

Several reports have appeared of congenital acquired megalo-ureter, associated with a permanent dilatation of the ureteric orifice and without a concomitant stricture, impacted calculus or other kind of obstruction.

Papin and Legueu (1912) reported four additional examples of congenital hydro-ureter similar to that of Saintu. They maintained that before a condition can be classified as congenital hydronephrosis, three criteria were necessary: 1) extreme dilatation and immobility of the ureteric orifice; 2) absence of interference with the continuity of the renal pelvis and the urinary bladder, and 3) complete filling of the ureter and renal pelvis with opaque medium following the same technique for the bladder. Eisenstaedt (1926) reported two similar cases.

ETIOLOGY

An attempt to explain the etiology of this condition requires a discussion of the term "megalo-ureter" and whether conditions thus classified really belong in this category. For example, if we are to follow the criteria set by Papin and Legueu, it must be definitely established that no mechanical obstruction is present. This, at times, may be extremely difficult unless painstakingly sought, as shown by Chwalla (1927). He found a possible cause for a dilated ureter in a vestigial membrane which he believed could function valvularly. Vermooten was inclined to agree with Chwalla's view as a result of a critical study of a number of ureteropyelograms. According to Campbell (1948) the term "megalo-ureter," formerly used, designated two distinct varieties, namely: 1) the kind described by Saintu and elaborated by Papin and Legueu, and 2) the form described by Caulk.

Theoretically, at least, the causes of this abnormality, as defined by Campbell, fall into three categories:

1) Obstruction. Although several theoretic varieties of occult infravesical ob-

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struction have been mentioned, e.g., urethral valves or vestigieal membrane (MacMyn), these possibilities can hardly be accepted in view of the absence of any visible obstructive lesions in any of the reported cases, and also because of examples of unilateral hydro-ureter reported by Hilliard.

In regard to conceivable occult obstruction involving the ureter itself, Bottomley attributed congenital ureteral ectasia to valve formation in the lower end of the ureter. Campbell, however, following a careful surgical search in four patients, failed to find any valvular formation or any evidence of stricture, as shown by Eisendrath, following the removal of the terminal segment of ureter from two patients. But Campbell believes that the cause of obstruction in the intramural part of the ureter is an acute angulation, probably caused by a downward pull of the dilated juxtavesical ureter.

We believe that in segmental ureteral ectasia some degree of obstruction occurs owing to a twist or kink in the ureteral wall occasioned by sagging of the dilated segment of ureter. The area of obstruction may be situated at the uppermost or lowermost part of the dilated segment. In the first instance, the ureteral catheter is frequently found coiled in the dilated segment of ureter; in the latter, it may be impossible or difficult to advance the tip of the catheter into the dilated portion of the ureter.

2) Neurogenic. The possibility of impaired innervation of the ureter was suggested by Thompson in a discussion of a report by Couvelaire. This assumption was probably based on a spinal cord lesion which, in turn, would result in an atonic bladder. Then again, if the assumption was a valid one, it would lead to bilateral ureteral ectasia. But since such premises have not been mentioned in reported cases, the possibility seems remote.

3) Developmental arrest. According to embryonic studies of Gerard, and also of Loraine, fetal ureters up to the fourth and fifth months are enormously dilated. The first appearance of muscle fibers in the ureteral wall occurs in the third month of intra-uterine life, arising in the juxtavesical part of the ureter and extending upward to the pelvis. Completion of the muscular layer occurs approximately in the mid-fourth month. Full muscular development of the ureteral wall corresponds closely to the time when the ureter is still in its dilated form. An arrest in development of the muscular layer may result in ectasia of a segment or even of the entire length of ureter, and may also involve the renal pelvis. Another possibility is the absence of normal inhibition of growth, which normally sets in after the fifth month of embryonic life, and results in the perpetuation of the dilated ureteral lumen throughout adult life. In my view this theory had definite merit as an explanation of the anomaly.

Campbell, on the other hand, found normal development of the muscular coat of the ureter in all specimens taken from his five patients, and thereby concluded that arrested development of the muscular layer is not the cause of this anomaly. He maintained that obstruction appeared to be the main cause of congenital megalo-ureter and that the term "congenital hydro-ureter" be reserved for conditions occasioned by obstruction, and "megalo-ureter" for examples presenting no evidence of obstruction.

The relationship between megalo-ureter and infection has been noted by many observers. When the infection begins in the renal parenchyma or pelvis, ureteral ectasia proceeds from above downward. The distal end of the ureter thus retains its spindle form for long periods of time. Eventually it may act as additional impediment to drainage and lead to further ectasia of the already dilated ureteral lumen. While this development may be true in a large percentage of patients, it is probable that infection may be the effect rather than the cause of the ectasia. Owing to impairment or absence of peristalsis in these megalo-ureters, pooling or stagnation of urine occurs above the intramural part of the ureter. This in turn may serve as an excellent culture medium for bacteria from the kidney.

SYMPTOMS

Symptoms directly attributable to ureteral ectasia are probably of little or no significance. However, in the event of superimposed infection or failure of the dilated ureters to empty into the bladder, symptoms may occur which are severe enough to warrant medical advice. The main symptoms, although not diagnostic, may be a sense of fullness in the loin or groin, increased urinary frequency, dysuria, fever and pyuria, the last-named becoming conspicuous with the onset of infection. To confirm the diagnosis of the anomaly it is necessary to resort to cystoscopic and pyelographic procedures.

A rigid, and especially a gaping, ureteral orifice is not invariably noted. Inability to advance the ureteral catheter into the renal pelvis, and coiling of the catheter in a segment of ureter, may suggest the diagnosis.

Urographic studies always confirm the diagnosis. Where there is a dilated, gaping and rigid ureteric orifice, reflux of the pyelographic medium from the bladder into the renal pelvis discloses the condition. When the ureteral orifice is unaffected and where sufficient renal parenchyma is present, the excretion of dye shows the defect clearly. Retrograde pyelography remains the only procedure in examples of complete parenchymal destruction and the presence of an apparently normal ureteral orifice.

TREATMENT

The treatment of choice for patients with unilateral involvement (when the remaining kidney is unaffected) is complete nephro-ureterectomy. In dealing with one who has a solitary kidney, acquired or congenital, or in whom the remaining kidney is impaired, the facilities available to the urologist are limited. When symptoms are absent or minimal, treatment may be unnecessary. Irrigation of the renal pelvis with a mild antiseptic solution and properly selected antibiotics may be tried when infection is present. Attempts have been made to transplant the affected ureter to another part of the bladder with the view of facilitating drainage. Plastic operations upon the affected ureter have been attempted with varying degrees of success, especially when ectasia is limited to a part of the ureter.

PROGNOSIS

The prognosis of unilateral megalo-ureter in a patient with a normal kidney on the opposite side is good following nephro-ureterectomy. In examples of bilateral involvement or solitary kidney, the prognosis is poor, or at best should be guarded because little or nothing can be accomplished except in palliation to improve drainage and minimize infection.

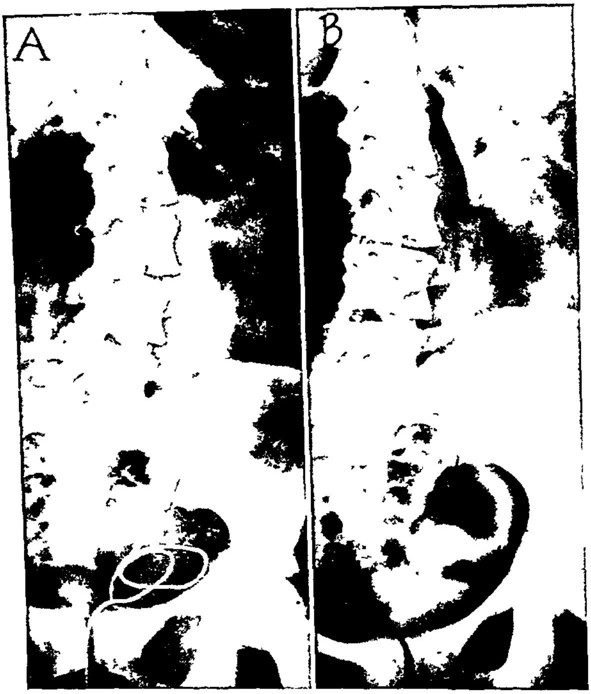

FIG 1 *A*, left shadowgraphy showing catheter coiled up in dilated lower segment of ureter *B*, excretory urogram. Note extreme degree of dilatation of lower third of ureter, with apparently normal pelvis and upper two-thirds of ureter.

CASE REPORT

Miss B. H., aged 43, a school teacher, first came under my care 12 years ago, complaining of attacks of left renal colic and hematuria of 3 years' duration.

Following a complete examination of the urogenital tract, a diagnosis was made of left renal calculus in a congenital solitary kidney. The lower third of ureter was extremely dilated. On September 3, 1938 the calculus was removed through a small incision in the pelvic wall. Convalescence was uneventful.

One year later patient returned for re-examination, stating that she experienced occasional left lumbar pain but no colic. Left shadowgraphy showed catheter coiled up in dilated lower segment of ureter (fig. 1, *A*). No recurrence of calculi. Phenolsulphonphthalein injected intravenously returned in good concentration from the kidney in 4 minutes, and urine specimen showed occasional leukocytes.

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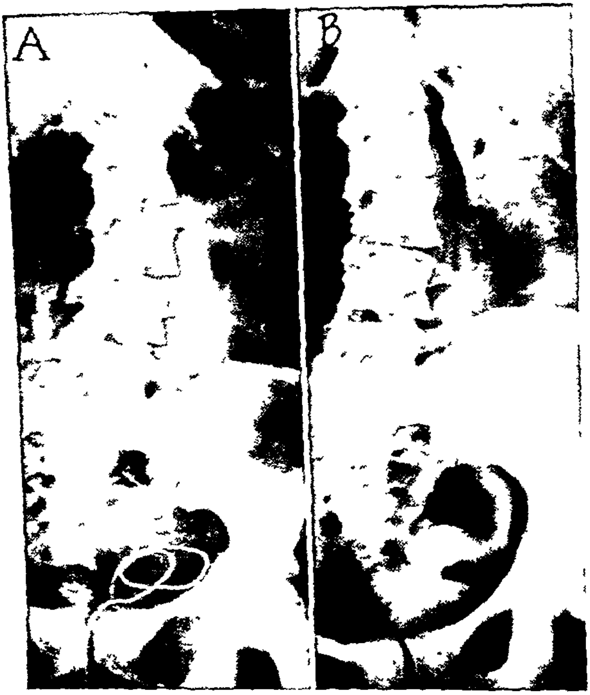

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For the next 5 years the patient felt little or no discomfort in the kidney, but December 14, 1944 she returned, stating that she had hematuria, left lumbar pain and increased diurnal and nocturnal urinary frequency. Cystoscopy disclosed mild cystitis; the left ureteral orifice appeared normal and showed normal peristaltic action. Ureteral catheter passed easily, but on x-ray was found coiled in lower ureter. Excretory urography showed extreme degree of dilatation of lower third of ureter, with normally appearing renal pelvis (fig. 1, *B*). The pelvis was completely filled 5 minutes after administration of dye, but failed to empty 75 minutes later. Urinalysis, negative. Specimens failed to show organisms on smear and culture. Blood chemistry showed no abnormality.

The patient returned 5 years later (April 22, 1949) for re-examination. She stated that, except for easy fatiguability, she had no urinary symptoms. Urologic survey showed the same conditions as were noted 5 years previously.

September 13, 1949 the patient returned, stating that for past 2 weeks she suffered pain in left lumbar region and left lower quadrant. Urinalysis now showed 2 plus albumin and several leukocytes. The urine was sterile bacteriologically.

On the morning of October 18, 1950 the patient experienced severe attack of renal colic. Urine was definitely turbid (pus). Cystoscopy again showed a normal ureteral orifice. Several attempts were made to pass a catheter to renal pelvis but each time the catheter coiled in the dilated lower segment of ureter. Phenolsulfonphthalein injected intravenously returned in good concentration in 12 minutes. The urine showed a growth of E. coli and B. pyocyaneus from the bladder, and E. coli from the kidney. The patient was given course of terramycin (250 mg. every 4 hours), and on November 14, 1950 a ureteral catheter was successfully passed into the renal pelvis, which was then irrigated with silver nitrate solution (1:500). Subsequent attempts to carry out pelvic lavage were unsuccessful owing to coiling of the catheter in dilated portion of ureter.

Operation (November 16, 1950): Under spinal anesthesia supplemented with sodium pentothal, cystoscopy was carried out. Two No. 6 ureteral catheters were passed into renal pelvis, following which lower ureter was exposed extraperitoneally through 6-inch Gibson incision. The lower third of ureter appeared saccular and approximated size of loop of small intestine. This ectatic segment of ureter extended from juxtavesical part to point approximately joining the middle and lower thirds of ureter. The lowermost part of dilated segment was so redundant that it overlapped juxtavesical ureter and resembled large diverticulum. The ureteric wall was greatly thickened. The mucosa appeared hemorrhagic. Several aberrant blood vessels extended from the hypogastric artery across the ureter. Adhesions bound the lower part of the ureter to surrounding structures, which were sheet-like and others like narrow bands (fig. 2).

The involved ureter was freed by dividing adhesions by blunt and sharp dissection and by ligating and dividing aberrant vessels. This severance was carried down to and into wall of bladder. A large elliptical segment of redundant ureteral wall was now excised. The defect was then closed over indwelling catheters with two layers of running 5-0 chromic catgut, passed so as not to include ureteral mucosa. The wound was closed in layers over large rubber dam and soft tube.

The left kidney was then exposed through 6-inch Albarran incision carried through old scar, and a Foley (20F) 5 cc bag catheter passed into the renal pelvis through small incision in the posterior wall of renal pelvis. The incision in the pelvic wall was closed around a catheter with two layers of 5-0 chromic sutures. The wound was closed in layers over a rubber dam and a tube placed in the renal fossa. A Foley catheter was introduced into bladder (fig. 3).

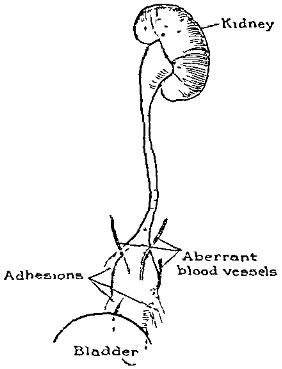

FIG. 2.

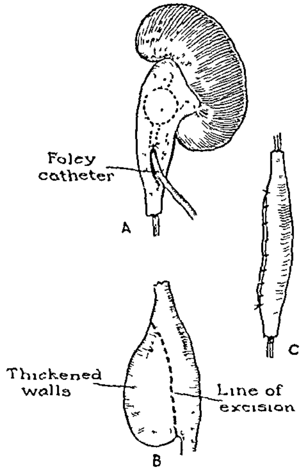

FIG. 3.

FIG. 2. Schematic drawing: extent of ureteral dilatation, aberrant blood vessels and fibrous bands.

FIG. 3. *A*, position of splinting ureteral catheters and Foley catheter in renal pelvis. *B*, line of excision of redundant portion of dilated ureter. *C*, closure of ureter over splinting catheters.

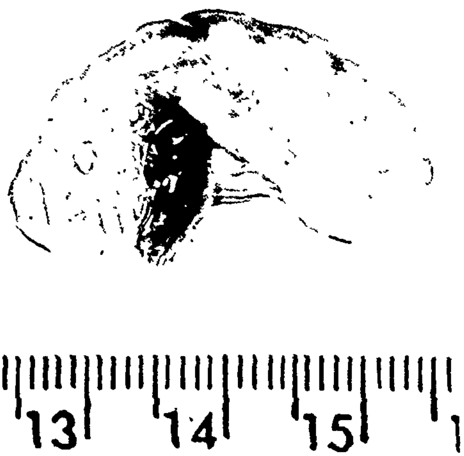

FIG. 4. Segment of ureter removed at operation

The urethral catheter removed on eighth postsurgical day and the ureteral catheter on the fifteenth day. Convalescence was completely uneventful and the patient discharged from hospital on the sixteenth day, with pyelotomy tube in situ, to be removed following period of ureteral dilatation to assure patency of reconstructed portion of ureter.

For the first 10 days following surgery the patient was given 600,000 units of aqueous solution of penicillin and 1 gm. streptomycin daily, and then 500 mg. terramycin daily for 6 days.

Pathologist's report (F. D. Speer, M.D., New York Medical College, Flower and Fifth Avenue Hospital): "*Gross specimen consists of one large mass of* tissue measuring 6 by 3 by 0.8 cm. It appears thick and brown, but cuts with ease (fig. 4).

"Microscopic: The ureteral wall is thick and shows subepithelial and intramuscular fibrosis which accounts for most of the thickening. There is slight muscular hypertrophy and minimal lymphocytic infiltration. Diagnosis: Marked *subepithelial fibrosis and slight muscular hypertrophy.*"

DISCUSSION

The history presented deals with a patient with a congenital solitary kidney who underwent a nephrolithotomy for renal calculus 12 years previously. At the time of the first examination, the lower third of ureter was found to be dilated. Although this condition progressed during the intervening years, the upper two-thirds of the ureter and renal pelvis failed to disclose evidence of dilatation. Symptoms were few and mild until a few months prior to surgery, when infection set in, causing loin pain, pyuria and increased urinary frequency. The ureteral orifice was apparently normal in appearance and function. There was no difficulty in passing a catheter through the ureteral orifice into the lower segment of ureter. However, the catheter almost invariably coiled in the dilated segment of ureter and could not be introduced into the renal pelvis. The cause of the obstruction at the upper end of the dilated segment, we concluded, was a kink produced by downward sagging of the heavy-walled, dilated ureter at the area of junction with the normal portion, thereby displacing the lumen of the unaffected segment.

In view of the fact that there was 1) no evident obstruction in the intramural part of ureter, 2) an obvious impediment to the free passage of a ureteral catheter into the normal part of the ureter, and 3) absence of dilatation above the ectatic part of the ureter, two problems presented themselves: What was the cause of the marked dilatation of the affected part of ureter? And, why did the upper ureter and pelvis remain unaffected?

It seems probable that the condition under discussion falls into the group of megalo-ureters described by Caulk, rather than that analyzed by Saintu, because of the absence of any of the criteria laid down by Papin and Legueu. In regard to the cause of the dilatation, the only cogent explanation appears to be that it is a congenital weakness involving all layers of the wall of the involved segment of ureter. Inasmuch as the pathologic report indicates the unusual thickness of the ureteral wall was attributable to fibrosis, and that there was only a moderate degree of muscular hypertrophy, the cause cannot be ascribed to developmental arrest of muscular development or to faulty innervation, because in either case the muscular layer would show atrophy rather than hypertrophy. In our view the high degree of fibrosis was a secondary manifestation caused, most likely, by frequent attacks of ureteritis which, in turn, induced stagnation of urine and subsequent infection. Another hypothesis which comes to mind is that the presence of aberrant vessels may have been instrumental in preventing the affected segment of ureter from elongating, with the result that it retained its fetal state of enlargement.

In explanation of the absence of ectasia of the upper ureter, it can be postulated that a kink produced by sagging of the dilated part of the ureter may have produced a valvular variety of obstruction which, while not preventing the free passage of urine from the renal pelvis into the dilated part of ureter, could have impeded regurgitation of urine back into the renal pelvis, thereby obviating dilatation.

The problem involved in treating patients with segmental megalo-ureter, particularly when associated with a solitary kidney, is a difficult one, and its solution must of necessity depend upon certain conditions. In the absence of symptoms, treatment is not warranted. When they occur and are sufficiently severe to require serious consideration, they are usually attributable to colic, infection, or a combination of both. Frequently patients falling into this category respond to conservative measures, such as the use of antibiotics and ureteral drainage. In patients with severe symptoms and in those where functional integrity of the renal parenchyma is in jeopardy, more radical measures must be resorted to. When only a short segment of ureter is involved, it may be feasible to excise it and reimplant the proximal end into another part of the urinary bladder. As a rule, however, the ectasia involves too much of the ureter to warrant this procedure. It may then only be necessary to resort to other measures, such as 1) pyelostomy, 2) uretero-intestinal implantation, 3) ureterocutaneous implantation, or 4) plastic procedures.

Of the aforementioned measures, one which requires most serious consideration is ureteroplasty. While not completely devoid of hazard, it has the great advantages of establishing pelviovesical continuity with the smallest risk of subsequent infection, and avoiding the vexation—physical and psychologic—of carrying cumbersome appliances. In order to accomplish a proper plastic operation, especially when dealing with the lowermost part of the ureter, it is desirable to mobilize it completely. In so doing, however, it is almost impossible to preserve the extrinsic vascular supply of the mobilized ureter. While the intrinsic vascularity is usually adequate, it is possible, at times, that necrosis may occur and the ureter become completely occluded as a result of fibrosis. For this reason it is desirable, when performing a tangential resection of the ectatic segment of ureter, to splint it with one or two large catheters which should be left in place for two to three weeks, and to supplement the procedure with a pyelostomy. The pyelostomy tube should remain in place until subsequent cystoscopic examinations show complete patency of the reconstructed ureter. This may require the wearing of a pyelostomy tube for several weeks or months, and carrying out ureteral dilatation at least for one year to accomplish ureteral patency.

SUMMARY AND CONCLUSIONS

Idiopathic megalo-ureter is an unusual anomaly and falls into two categories: 1) the ureter solely is ectatic and the renal pelvis normal, a condition first described by Caulk; and 2) the ureter and renal pelvis are involved (most common variety). In the latter the ureteral orifice is patulous and there is absence of peristalsis, permitting free reflux from the bladder to the renal pelvis.

Although some authorities have reported, after careful examination, the discovery of a valvular obstruction in the ureter or urethra, this has not been generally confirmed. Several theories have been advanced to explain the anomaly, but none is entirely satisfactory.

The condition may be unilateral or bilateral. The lesion rarely involves a segment of one ureter. Symptoms may be entirely lacking. If present they are usually caused by superimposed infection, or to pain resulting from obstruction owing to impairment of drainage. Diagnosis is made by urography.

Treatment depends upon: 1) presence or absence of debilitating conditions; 2) unilateral or bilateral lesion; 3) jeopardy to vital renal parenchyma. Treatment is not indicated in the absence of severe symptoms. Antibiotics and ureteral catheter drainage usually suffice to relieve symptoms consequent upon infection and impaired drainage.

When surgical intervention becomes urgent, nephro-ureterectomy is the procedure of choice if the involvement is unilateral and the remaining kidney shows adequate function. For patients with bilateral involvement, or when dealing with a lesion in a solitary kidney, the choice of procedures is: 1) permanent pyelostomy; 2) uretero-intestinal anastomosis; 3) cutaneous ureterostomy; 4) excision of involved segment of ureter and re-implantation of the remaining ureter into another part of the bladder (a procedure rarely possible), and 5) ureteroplasty.

The hazards, advantages and technical details involved in accomplishment of ureteroplasty are described. Segmental ectasia of the ureter in a patient with a congenital solitary kidney successfully treated by ureteroplasty is reported.

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PRIMARY URETERAL TUMORS

MORRIS R. KEEN

This presentation of 6 cases of primary ureteral tumors (five malignant and one benign) is concerned with the present incidence, the associated clinical problems, and an evaluation of the pathogenesis in the light of present knowledge. In the latter group, our own pathological studies in five of these cases will be contributed.

In 1939, our first case of primary ureteral carcinoma was presented. The literature then had recorded 150 cases, two-thirds of which had been observed in the preceding 8 years. The data of large medical centers in 1939 revealed the following:

3 cases in 22,000—Johns Hopkins Hospital
1 case in 22,000—Bellevue Hospital
1 case in 7,700—Ohio State University Hospital
4 cases in 13,800—Vienna Anatomical Institute

Mortensen and Murphy (1950) collected 245 cases of ureteral malignancy and added six others (three malignant and three benign). Vest in 1945 found 75 cases of benign tumors. These figures must be interpreted as an approximate evaluation as the reviewer is bound to overlook some cases on record.

Since 1939, five additional ureteral tumors have been seen in a practice serving a rural-suburban community. Three of these tumors were observed in a single hospital of 100 bed capacity. Based on the number of urological cases seen in the eleven-year period, the incidence would approximate 1:1300. An additional case of multiple primary ureteral malignancies of varying degrees has been seen.

As expressed by Braasch (1939) and Fagerstrom (1950), "all this is indicative of an awakened awareness on the part of the urologist, aided by progressive improvement in diagnostic technique."

CASE REPORTS

Case 1. A 59 year old man (J. W. S.) presented right renal colic, frequency and urgency. Past history: Suspected tuberculosis of left lung, sinusitis and bronchial asthma; typical pyelo-ureterogram (fig. 1). Clinical crises were characterized by severe bronchial seizures with exodus 6 weeks after onset of mild urological symptoms. Autopsy revealed metastases to lungs, liver, mediastinum and left kidney.

Case 2. A 47 year old man (C. S.) had hematuria following the lifting of a heavy automobile tire. With bed rest, the hematuria ceased but recurred with resumption of work. A right retrograde pyelogram disclosed a filling defect suggestive of either tumor or uric acid calculus (fig. 2). The patient was treated for ureteral calculus and subsequently passed a hard gritty substance (old blood clot). Re-examination established definite diagnosis of primary ureteral tumor. Nephrectomy with partial ureterectomy was performed elsewhere. Pathological diagnosis: Papillary

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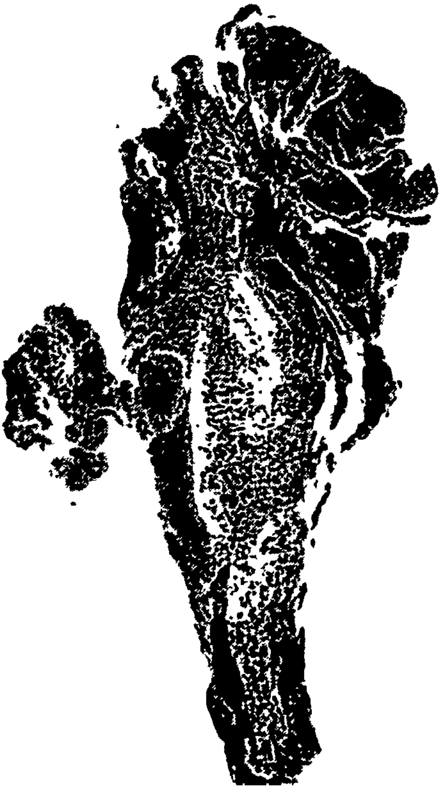

FIG. 1

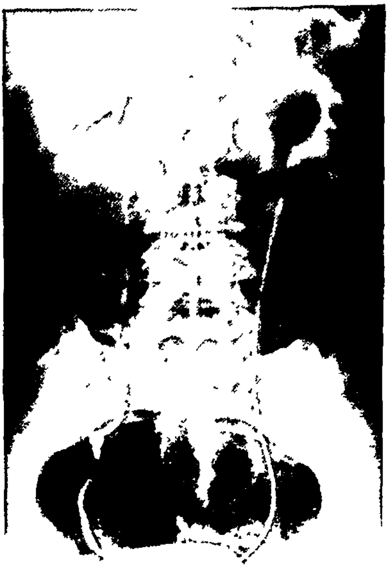

FIG. 2

epidermocarcinoma of ureter. Eight months later, vesical recurrence ensued with subsequent ureterectomy and partial cystectomy (M. R. K.). Nine months of good health were followed by marked spasm of the sacrospinalis muscle, bilaterally, and impaired extension of the right lower leg.

Subsequent laminectomy and cordotomy were performed with only partial relief from pain. Gross examination of the spinal nerves and associated structures revealed no evidence of metastases. The patient's course was progressively downward. Prior to exodus, a metastatic mass developed in the right inguinal area and right scrotal sac. Biopsy of this area was identical with the original ureteral tumor.

Summary: This case presented several disturbing features: 1) a question of determining causal relationship between trauma and the hematuria which ensued; 2) the futility of urological surgery in preventing complications; 3) the development of severe neuro-orthopedic complications not responding to neurosurgery or deep x-ray therapy; 4) the unusual mode of extension of malignancy along the spermatic cord into the scrotum.

Case 3. A 55 year old man (A. G.) in 1948 had painless hematuria, which was secondary to a pedunculated papillary tumor (2 cm.), above the left ureteral orifice. The tumor was treated by transurethral resection and radon seed implantation. A bilateral pelvic sympathectomy for Buerger's disease was performed in 1949. A normal twenty-six month postoperative period followed. Routine cystoscopy then disclosed a cigar-tip shaped lesion protruding from the right ureteral orifice, which descended into the bladder with each jet of urine and receded between times. Excretory urogram revealed a moderate right hydroureter. Biopsy of the ureteral tumor and previous bladder tumor were both reported papillary carcinoma.

A right nephro-ureterectomy with a cuff of the bladder was performed. The site of the ureteral orifice and intramural area previously were fulgurated.

Gross and microscopic examination of the removed kidney and ureter revealed no evidence of any tumor. The fulgurated area presented some edema and a few associated subepithelial cysts.

The multifocal origin of transitional epithelial tumors is well illustrated here. The question was raised whether the tumor seen at the right ureteral orifice was of ureteral origin. The behavior of the lesion during the ureteral peristalsis convinced us of its ureteral origin.

A case of bilateral ureteral malignancy has been reported by Ratliff, Baum and Butler. Macalpine presented 2 cases of bilateral renal papilloma, and quoted four additional ones of bilateral renal pelvic tumor involvement. (Rager, 1841; Murchinson, 1870; Retzloff, 1904; Maybury and Duke, 1925). Thomas and Regnier (1924) studied a series of 248 cases of tumor of the renal pelvis and ureter and found bilateral involvement in 4.2 per cent.

The mode of treatment of this ureteral malignancy presented several possibilities: 1) local fulguration; 2) deep x-ray therapy to all transitional epithelium, followed by local fulguration as suggested by Bothe; 3) a nephro-ureterectomy and cuff of the bladder.

Surgical elimination of the right kidney, ureter and the cuff of the bladder was selected because of the type of cellular malignancy and the known experience of recurrence in the remaining ureteral epithelium.

Counseller, Cook and Seefeld elected to fulgurate a ureteral tumor at the ureteral orifice in a patient with severe pulmonary tuberculosis. Kajen and Petkovic record a similar case of papillary carcinoma of the ureter treated with cystoscopic fulguration in a patient who refused surgery and remained well for over a period of 14 years.

Bothe's suggestion of deep x-ray therapy to transitional epithelium (bladder) followed by fulguration was based on clinical experience of no recurrences in two cases of bladder tumor treated by preliminary x-ray exposure. In 2 cases treated by fulguration alone, recurrences were constant.

Case 4. A woman aged 71 (A. A.) in 1949 complained of painless hematuria of 1 week's duration and some weight loss. A preliminary excretory urogram showed delayed function on the right side with some dilatation of the right renal pelvis. The region of the lower right ureter presented two calcific shadows, 2 cm. and 1 cm. in diameter (fig. 3, *A*). A plain urogram with a catheter in situ showed the tip of the catheter to be impinged at the level of the smaller of the two calcific shadows (fig. 3, *B*). A diagnosis of right hydronephrosis associated with right ureteral calculi was made.

Cystoscopy and a right retrograde pyelogram showed a filling defect in the right lower ureter (fig. 3, *C*). The opacities previously noted and assumed to be in the ureteral path had shifted and were definitely extra-ureteral. Right nephroureterectomy with partial cystectomy was performed with an uneventful outcome.

Pathological diagnosis: Polypoid transitional carcinoma of the ureter, grade 2, associated with lymphatic invasion.

This case is of interest because of the confusing association of opaque shadows in the line of the ureter interpreted as stones. Calculi associated with ureteral tumor on the same side and on opposite sides have been reported by Mortensen and Murphy, Burnell and Brooks. Lazarus noted their presence in ten out of 68 ureteral tumor cases. Scott believes that with the ureteral catheter it is possible to distinguish between resilience of tumor tissue and the more definite obstruction of stone or stricture.

Case 5. A 61 year old woman (MacB.) was seen by Dr. Carl Schmidlapp for recurrent hematuria, low backache with pain in the upper right quadrant. The presence of a ptotic kidney was known for years. Cystoscopic examination (C. S.) showed a normal left ureteral orifice. A right pyelo-ureterogram revealed right hydronephrosis, right hydro-ureter with obstruction at the pelvic brim, and marked stricture formation of the lower two inches of the ureter. Minor calyces showed bizarre, fuzzy appearance (fig. 4).

Diagnosis: 1) Right hydronephrosis, hydro-ureter, associated with obstruction at the pelvic brim, apparently extraureteral; 2) acid fast infection is the second possibility; 3) a tumor of the ureter has not been excluded.

Exploratory and right nephrectomy (C. S.) performed revealed a definite tumor of the lower ureteral segment with pelvic gland infiltration. Pathological report: Transitional cell carcinoma of the ureter, grade 2, with lymphatic invasions.

Interpretation by roentgenologist: A stricture of the lower right ureter, acid fast in origin, is suggested.

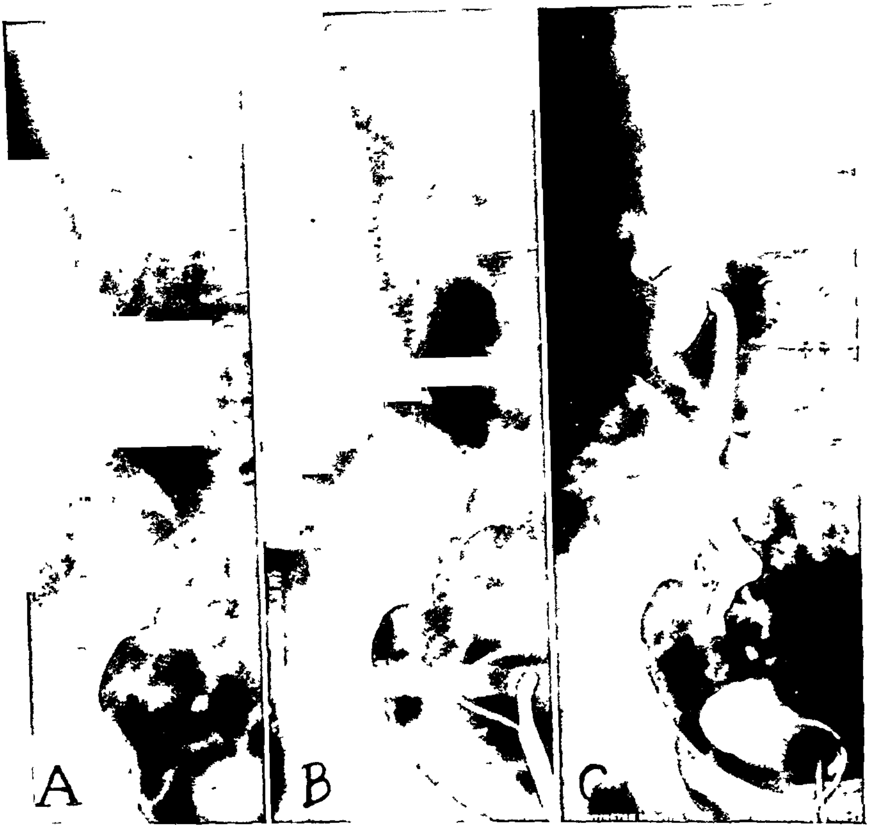

Fig. 3. *A*, showing two calcific shadows, 2 cm and 1 cm. in diameter, in region of lower right ureter. *B*, showing catheter tip against calculus? *C*, right retrograde pyelogram showing filling defect in right lower ureter Opacities previously noted and assumed to be in ureteral path, had shifted and were definitely extra-ureteral.

This case is of interest because the pyelographic outlines presented the possibility of an acid fast lesion to a competent roentgenologist and urologist.

Case 6. A 55 year old woman (M. S.) in 1949 had profuse hematuria 1 week after a supravaginal hysterectomy for bleeding uterine fibroids. Possible ligation of the ureter was considered by the surgeon. Cystoscopic examination showed a patulous left ureteral orifice. A No. 5 catheter passed easily to the left renal pelvis, from which blood tinged urine flowed rapidly. A left pyelo-ureterogram showed moderate hydronephrosis and a definitely annular constricting area in the lower ureteral segment (fig. 5). A preliminary excretory urogram showed a normal right kidney and ureter. Delayed function was noted on the left side. Diagnosis: Constricting annular tumor of lower left ureter.

Nephro-ureterectomy with partial cystectomy was performed. Pathological report: Chronic pyelonephritis; moderate dilatation of the pelvis and ureter; benign papilloma at lower segment associated with peri-ureteritis.

This case is of interest in presenting a differential diagnosis between operative ligation of the ureter, or constricting tumor of the ureter. A review of the patient's history revealed the presence of low backache for years, and some mild urinary symptoms.

Routine excretory urography should be performed in the presence of enlarged uterine fibroids. Some of the information thus gathered would be revealing.

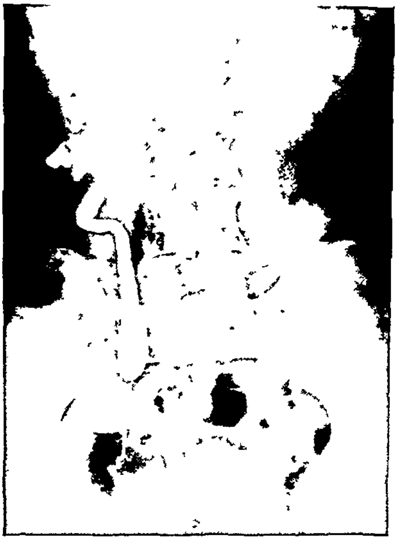

Fig. 4.

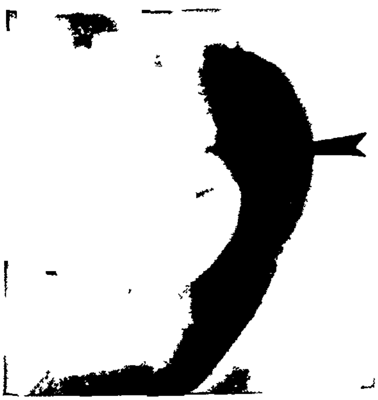

Fig. 5.

Fig. 4. Note fuzziness of minor calyces and stricture of ureter
Fig. 5. Note annular constriction of ureter

Harrison, Warres and Fust collected a series of 10 cases of primary ureteral tumors and emphasized the following features: 1) the cessation of hematuria with nonspecific therapy and subsequent delay in adequate urological investigation. 2) Resection of a pelvic tumor with re-anastomosis and subsequent tumor recurrence in the bladder and remaining ureter; 3) the frequent initial treatment of bladder papillomas and tumors secondary to ureteral origin; 4) the presence of pain from metastases as a first sign; 5) since these tumors occur chiefly in the male (2.1) and reach their highest incidence in the prostatic era (50 to 70 years), complete visualization of the upper urinary tract should be a required preoperative determination in all candidates for prostatic surgical evaluation.

The author's series of six ureteral tumors serves to indicate the following: 1) the insidious character of ureteral tumors; 2) the confusing pyelographic outlines which can result; 3) the multicentric origin of these tumors and the problem of their management; 4) that routine pyelographic investigation should be employed in diseases of the uterus and adnexa.

PATHOGENESIS

The pathogenesis of ureteral tumors offers a stimulating and provocative field for study. Why is the transitional epithelial lining of the urinary tract the site of multicentric tumor growth? What directions do the growths take? What forces determine the same?

The etiological factors associated with epithelial ureteral tumors mentioned in the past are leukoplakia, ascending epidermization, mechanical irritation (stone), chronic inflammatory processes, benign mucosal hyperplasia with eventual malignant change.

Recent emphasis has been on avitaminosis, hormone imbalance, toxic products of metabolism, specific carcinogenesis, virus infection.

A detailed evaluation of the experimental and clinical supportive data for the above group is not the purpose of this paper. A study of the literature does convince one of the rationale and validity of the premise that the transitional epithelium of the urinary tract can be stimulated to produce single or multiple tumors by one or a combination of these factors.

Ever since Limbeck (1887) and von Brunn (1893) called attention to the infolding of transitional cell epithelium and resulting pinched-off areas in the subepithelial layer, attention has been focused upon these zones (buds, cell nest, cysts or glands) as the anlage for possible malignant growth. True or apparent secretory activity has been described in these areas. Subsequent excellent investigations have substantiated the presence of these inclusions in considerable numbers of all levels of the upper urinary tract and bladder. A majority of these present associated inflammatory reaction.

Recently Fagerstrom, in a detailed study of pelvis and ureters of 120 unselected autopsy cases, presented these significant conclusions and findings:

1) Cell nests and buds are but bizarre expression of epithelial hyperplasia resulting from chronic infection and noxious agents in circulatory fluids.

2) Excessive activity of epithelium induced by unknown factors may result in hyperplasia, widespread or isolated. The isolated areas in turn can assume a papillary excrescence or a downgrowth into loose connective tissue of the subepithelial zone. This downward focal proliferation is augmented by increased hydrostatic pressure and ureteral contractions. Papillary new growths are extremely rare as compared with the incidence of buds.

3) Buds or crypts were *not* found in persons below 20 years of age.

4) All buds or nests have a connection with the surface epithelium, thereby confirming the work of Stirling and Ash.

5) Crypts or buds exist as one or the other in the majority of cases; co-existence is infrequent.

6) Also seen were microscopic inflammatory changes evidenced by edema, new capillary formation and epithelial hyperplasia, but no leukocytic infiltration or bacterial invasion.

7) A great degree of vascularity associated with bud formation (epithelial hyperplasia) makes von Brunn's theory of central necrosis of buds highly vulnerable.

8) Cysts arise from occluded mucosal crypts, rather than from buds.

9) No secretory structural cells were found in the ureter.

However, Foote did report a glandular type of epithelium in three renal pelves and one ureter. In these cases he noted "a complete replacement of the transitional epithelium by a thick red velvety membrane. Microscopically this membrane had the appearance of intestinal mucosa." N. J. Jacob, Jr. and Mau reported 2 cases of pelvic, ureteral metaplasia towards intestinal mucosa and in one instance associated with malignancy. The factor of multiplicity of ureteral tumors may be explained on one or more of the following bases: 1) lymphatic permeation; 2) surface implantation; 3) multicentric origin.

Lymphatic permeation can be discounted as there is little or no pathological support. Most proliferative epithelial tumors grow at a surface level.

Surface implantation is supported by the clinical observation that these tumors do not arise in haphazard fashion as a rule, but follow the path of urinary flow and peristalsis. A few isolated cases of implantation are recorded in a direction opposite to the normal flow of urine (Rogers, Mortensen and Murphy). Obstructive factors at any level may localize the spread. Over half of the primary ureteral tumors are at the lowest segment of the ureter. The narrowed lumen of the intramural ureter may create a temporary stasis of urine and thereby greater concentration of the urocarcinogenic factor upon the adjacent mucosa. Masina reports 40 cases of primary ureteral tumors (5 per cent of his series) situated in the last inch of the ureter, at the following sites: juxtavesical, intramural, submucosal.

The multicentric origin also has clinical support. Multiple growths of different cellular components in opposite ends of the ureter and pelvis have been recorded. The recurrence of ureteral carcinoma in the remaining ureter after local excision of a tumor area is well known.

Willis, in his excellent work on *Pathology of Tumors*, aptly summarized the present status by saying that "when a carcinogenic factor is applied to tissue, it is not applied to a single focus but to a more or less extensive field of the tissue. Visible tumor formation usually commences at one or more small foci in that field, but the neoplastic change extends from these to the other parts of the field."

The causal relationship between epithelial buds and ureteral malignancy has been explored by Bothe (1943) and Fagerstrom (1950). Prompted by a review of the pathological findings in the bladders of aniline dye workers and the stomachs of mice after the ingestion of carcinogenic hydrocarbons, Bothe studied 6 primary tumors of the ureter and four of the renal pelvis. He saw similar changes in and about areas proximal to and remote from the tumor sites. Grossly, these areas were either normal in appearance, slightly granular, or ulcerated. Microscopically, these changes consisted of varying degrees of round cell infiltration, submucosal hyperemia, epithelial layer thickening, surface digital penetration, and papillary formation.

Bothe felt that in his series of cases the changes observed in the ureters and pelves were not unlike those in the human bladder of aniline dye workers, as demonstrated by Gay. Therefore, he postulated that "on hypothetical grounds, inflammatory areas illustrated early reaction to carcinogenic stimulation while areas of proliferating basal cells were more advanced lesions eventually becoming papillary and definitely neoplastic."

While acknowledging this preceding statement to be mere conjecture, it seemed within the "bound of possibility to assume intramural changes starting in basal layers as due to irritants or carcinogenic agents excreted by kidneys or transmitted by blood or lymph."

Everett and Wayburn presented a case with diffuse infiltration of the renal pelvis and ureters by von Brunn "cell nests." In one single area, they found "a very suggestive, extremely early squamous cell carcinoma." The finding of a single questionable area of suspected malignancy in diffuse subepithelial cell nest distribution makes one speculate as to the true causal relationship. Especially is this so, when the extensive areas probably are subjected to the same carcinogenic factors in the urine.

Fagerstrom studied four surgical specimens (two primary ureteral tumors and two of the renal pelvis) with the same objective. Three showed no cell buds or crypts in the uninvolved portion of the ureter and pelvis. In one case with a diffuse distribution of cell buds throughout calyceal-pelvic-ureteral epithelium, none could be found underlying the tumor bearing area. No evidence could be found "that solid epithelial buds are directly associated with the origin of solid tumors of the urinary epithelium" in any of his cases.

The question of causal relationship between the subepithelial inclusions (buds) and malignancy has also intrigued the writer. Five similar surgical specimens (four of ureter, one of renal pelvis) have been examined along the pattern outlined by Bothe and Fagerstrom. The following tabulation illustrates the findings in this series:

Subepithelial cell inclusions

CASE	LESION	SITE OF TUMOR	PROXIMAL URETER	MID PORTION OF URETER	REMOTE URETER	RENAL PELVIS	CHRONIC INFLAMMATION
A. G.	Pap. ca. *l.u.	**−	−	−	**+	+	+
MacB	Pap. ca. l.u.	−	−	−	−	−	+
M. S.	Pap. l.u.	−	−	+	+	+	+
A. A.	Pap. ca. l.u.	−	−	−	+	+	−
M.	Pap. ca. 2 r.p.	+	−	−	+	+	+

* l.u.—lower ureter
r.p.—renal pelvis
** − none present
+ present

In 1938, Hueper's classical review of aniline bladder tumors presented detailed and systematic histological descriptions of early (pre-cancerous?) and neoplastic changes in humans and dogs. Four types of nonneoplastic changes were noted.

1) Inflammatory reactions (simple and ulcerative) as precursors of the development of neoplastic conditions.

2) Intra-epithelial abnormalities which consist of localized changes in the morphological character and arrangement of the epithelial cells.

3) Leukoplakia (simple, papillary and infiltrative).

4) Mucus polyps (simple, papillary and infiltrative).

If transition does occur from these subepithelial inclusions (buds) to actual carcinoma, one might expect some demonstration of these changes as outlined by Hueper.

In my series, no such evidence could be found. One case of papillary carcinoma of the renal pelvis showed a solid row of subepithelial buds or cell nests but no breakthrough at the site of the tumor bases. The chronic inflammatory changes present consisted of round cell infiltration and were found in four out of five cases. It was believed that this process was nonspecific in nature.

For further enlightenment in the pathogenesis of ureteral tumors, one should turn to the series of special stains studies for Golgi material and mitochondria presented by Bothe in 1950 at the American Urological Association's annual meeting. This study was concerned with the distribution of the Golgi material and mitochondria in benign and malignant cells of the urinary tract.

Although known for some fifty years (Golgi, 1898) to the biologist and pathologist, the Golgi apparatus and mitochondria elements of the cell are relatively unknown fields of knowledge to the practising urologist. Therefore, a brief description would be in order.

The Golgi material of the cell represents a portion of the cytoplasm vitally concerned with elaboration of proteins, lipoids, pigments, hormones and vitamins. Secretory granules are also formed. The mitochrondria has a similar origin but is said to be more stable, also more constant in chemical composition.

The Golgi substance is a constant constituent of the cell but can assume a variety of forms depending on the reaction to the stain fixation processes. Two components of Golgi substance are known, a) chromophilic and b) chromophobic. Each in turn can be primary protein or lipoid in composition. The chromophobic factor, when composed of fat, passes to the lighter end of the cell. When essentially protein in makeup, it may move to the opposite end. The chromophilic component may go to any part of the cell. It is this migration of the Golgi apparatus and the mitochondria to various parts of the cell which created a definite pattern after special fixing and staining processes.

In a study of 152 benign prostatic hypertrophy cases and 32 cases of prostatic carcinoma, Bothe, Dalton and associates were able to observe a very significant and constant distribution of the Golgi material and mitochondria in both benign and malignant cells.

The Golgi material in benign cells precipitates or locates itself at the free end of the cell in juxtanuclear position, as a heavily impregnated strand. This strand may extend towards the lateral borders of the nucleus in the direction of the base of the cell.

In malignant cells, there is a reversal of the Golgi material away from the free surface to the other side of the nucleus, more of the cytoplasm is invaded. The mitochondria also presents a different distribution pattern on staining.

In benign cells the mitochondria can be seen as either short large filaments or spheres, few in number, concentrated in the cytoplasmic area between the nucleus and the free border of the cell. In the malignant cell, the pattern consists of numerous small tenuous filaments and spheres.

The specificity of these benign and malignant patterns was of especial interest to me since I thought that such stain studies could be utilized for possible enlightenment as to the origin of multicentric ureteral tumors. Personal communication with Bothe as to the hypothesis outlined above elicited the following: "It is our feeling, however, that some of these (transitional cell and subepithelial buds) will show changes in a non-involved area before the actual neoplastic hyperplasia has been established. This is very hypothetical, and will require considerable study."

It was our intention to apply these special stains to the ureteral material on hand. Due to technical difficulties, such studies could not be completed. The character of Golgi material and mitochondria is such that fixation of the tissue in Champy fluid must occur within ten to fifteen minutes after the blood supply to the organ is severed. Dr. Bothe has the technician in the operating room for immediate fixation.

It is hoped that this paper may alert others in the use of these stains toward a better understanding of the pathogenesis of multicentric tumors of the urinary tract. Perhaps a "central depot" of investigation could be established.

SUMMARY

Six cases of primary ureteral tumor (five malignant and one benign) are presented.

An incidence of 1:1300 is noted.

Associated clinical problems are presented.

A study of the causal relationship between ureteral carcinoma and subepithelial cell nest or buds could not be established in this series.

Special stain studies of the Golgi material and mitochondria will be necessary for further enlightenment of the pathogenesis of primary ureteral epithelial tumors.

Thanks are expressed to the referring physicians whose patients have made this study possible (Dr. C. Bernstein, Dr. D. Currie, Dr. Gross, Dr. J. L. Sengstack, Dr. T. M. Winston).

I am greatly indebted to Dr. Herbert Holleb, Director of Clinical Laboratories at Huntington Hospital, for the major preparation of the pathological material and its interpretation. My thanks are also expressed to Dr. Louis E. Marshall, Pathologist at Southside Hospital, Bay Shore, N. Y., and to Dr. Carl Schmidlapp for making case record MacB available.

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PRIMARY URETERAL TUMORS WITH A REVIEW OF THE LITERATURE SINCE 1943

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Primary ureteral tumors are no longer the rarity they once were considered, but rather have graduated into the "not uncommon" classification. Ureteral tumors would be more common if greater effort would be made to discover them. With improved modern urologic implements, roentgenograms, and laboratory techniques, there is much greater opportunity for the early diagnosis of this entity. It is our purpose to evaluate the best methods of diagnosis, and to see if there has been any change since W. W. Scott's memorable article in 1943. We plan to offer a simple, rational system for your approval, on the diagnosis and treatment of primary ureteral tumors.

The original description of ureteral tumors was by a Frenchman, Rayer, in 1841. The first report, in English, was in 1884, by Davy. Foord and Ferrier report only 8 cases recorded in the literature by 1900, and these were all on post-mortem examinations. It was not until 1902 that Albarran made the first preoperative diagnosis. By 1934, sixty-one cases had been found, and in 1943, Scott found 180 cases and added two. Gualtieri, Hayes, and Segal in 1948 brought the total cases reported in the literature to 196. As late as May, 1951, Taylor stated that 207 cases were published. Since Scott's report in 1943, we have found 128 cases in the literature. We wish to add 2 cases of our own, thus bringing the total to 310 cases, as of May 1951. A few more case reports are listed but, because of library difficulties, they were not obtained.

EMBRYOLOGY

Fagerstrom, in his interesting discussion of the origin of primary ureteral tumors, states that urinary epithelial hyperplasia is due to local irritation from chronic infection, or noxious agents in the body fluids. This sharply disagrees with von Brunn's theory of "cell nests" as the site of origin. Fagerstrom states that epithelial buds and crypts are but bizarre expressions of epithelial hyperplasia. Melicow, in 1945, after an embryological, histological, and clinical investigation, stated that all urinary tract linings should be called "urothelium" because of their similarity. This would distinguish it from the gastro-intestinal tract's mucous membrane, and the epithelium of the skin. He believes that all urothelial tumors should be grouped together because of this. We agree with this urothelial theory. Previous articles have never given this over-all picture, but rather have been separated into gross structures (i.e., kidney pelvis, ureter, and bladder). This makes a rational evaluation very difficult, if not impossible. We are therefore presenting only primary ureteral tumors.

CASE REPORTS

Case 1. (Patient of Dr. John J. Bottone, L.I.C.H. U-52489.) Mrs. L. R., a 58 year old married white woman, was first admitted to the Long Island College

Hospital on August 28, 1950 with the chief complaint of right flank pain, off and on, for 3 months. Her past history was noncontributory other than a "repair of the uterus" (questionable uterine suspension) in 1928. She claimed to be perfectly well until 3 months before admission, when a dull, nonradiating pain in the right flank occurred for 10 minutes a day. This increased to 12 hours a day and became more severe for the 2 months prior to admission. Two weeks before admission, hematuria, frequency, and nocturia 2 times developed. The system review was negative. Physical examination revealed the following positive findings: obese, white female, with tenderness over the right lower pole of the kidney. Her liver was one to two finger breadths below the right costal margin.

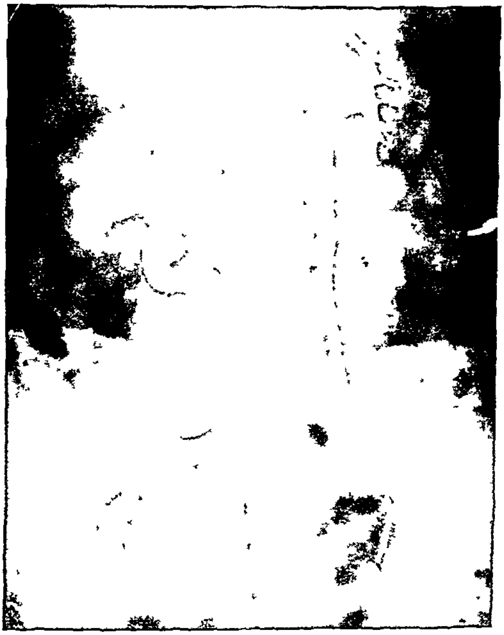

Fig. 1. Retrograde pyelogram showing right hydronephrosis and hydro-ureter entire length of ureter.

Laboratory findings: Complete blood count, normal. Urinalysis: pH, 5; specific gravity, 1.008; albumin, 1 plus; sugar, 0; acetone, 0; microscopic, 3 white blood cells per high powdered field, culture negative. Urea, 35.5 mg. per cent; sugar 84.0 mg. per cent; serology negative.

Cystoscopy was not remarkable except for right ureteral obstruction at 10 centimeters. Retrograde pyelogram showed a marked right hydronephrosis and hydro-ureter (fig. 1) with no evidence of calculi present. The cause of the ureteral obstruction was thought to be due to ureteral damage done at the previous gynecological procedure. A nephro-ureterectomy was performed with removal of 15 cm. of the proximal ureter. Marked hydronephrosis and hydro-ureter were present but no evidence of tumor was present in the kidney or ureter. The patient was discharged on the twelfth postoperative day in good condition. The patient was asymptomatic for 3½ months, when she had a recurrence of hematuria, but no other urinary complaints. Cystoscopy at this time revealed a small, round, smooth mass protruding from her right ureteral orifice. A biopsy taken from this mass was reported as a grade 3 transitional cell carcinoma of the ureter (fig. 2, *A*). The pathological report was as follows: "Invasion of the fibrous tissue by nests of tumor cells. The tumor is of transitional type with cells of moderate size. The nuclei are ovoid or round, and are hyperchromic with one mitotic figure per high power field. No keratinization is seen."

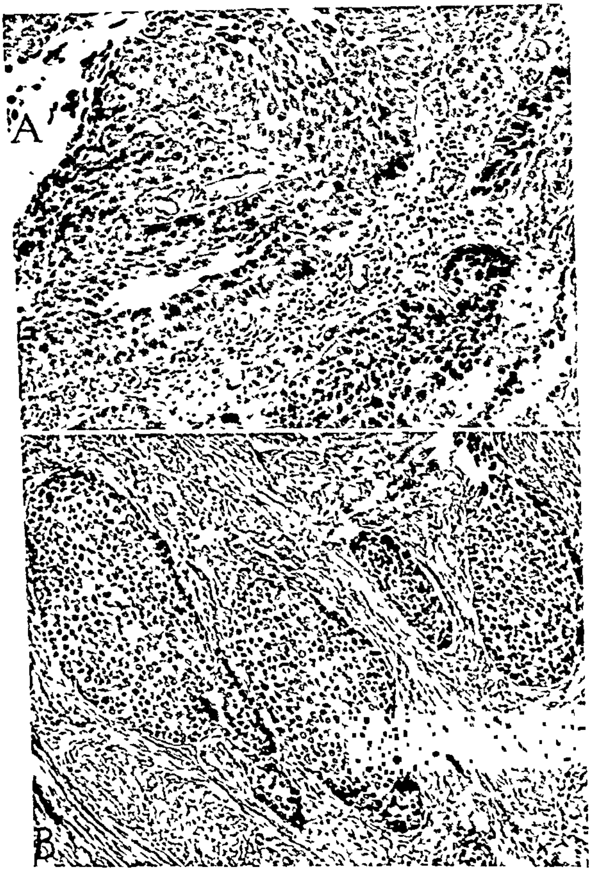

FIG. 2. *A*, transitional cell carcinoma of ureter. Tumor cells occur as solid nests infiltrating submucosa. Five mitotic figures are seen. *B*, transitional cell carcinoma of ureter. Solid nests of tumor cells are seen invading muscularis.

A ureterectomy and partial cystectomy were advised, but the patient refused for 7 months, preferring to have monthly fulguration of the ureteral protrusion of the tumor. Finally, on June 14, 1951, ten months after the nephrectomy, a ureterectomy and partial cystectomy were performed. A review of the section taken for biopsy was compared with the slide of the operative specimen slide showed a similar transitional cell carcinoma, grade 3 (fig. 2, *B*). The postoperative course was uneventful except for a slow-healing abdominal wound. She was discharged on her twenty-eighth postoperative day for x-ray therapy as an "out" patient.

Since the patient was just discharged from the hospital, no follow-up is available.

Case 2. (Patient of Dr. E. King Morgan, L.I.C.H., U-55260.) Mr. J. McR., a 54 year old white man, entered the Long Island College Hospital for the first time on December 18, 1950, with the chief complaint of "blood in his urine for ten days." Five months before admission, several episodes of painless hematuria occurred accompanied by long, slender blood-clots. This condition was worse in the morning and cleared up by evening. These attacks lasted two to three days, occurring every two weeks for a month. Cystoscopy by a competent urologist elsewhere was reported as negative. The patient lost 13 pounds over the following 3 months, with no other complaints. For the 10 days prior to admission, the patient had persistent hematuria with clots. Accompanying this was dysuria, urgency, frequency, and pain in the left groin during micturition.

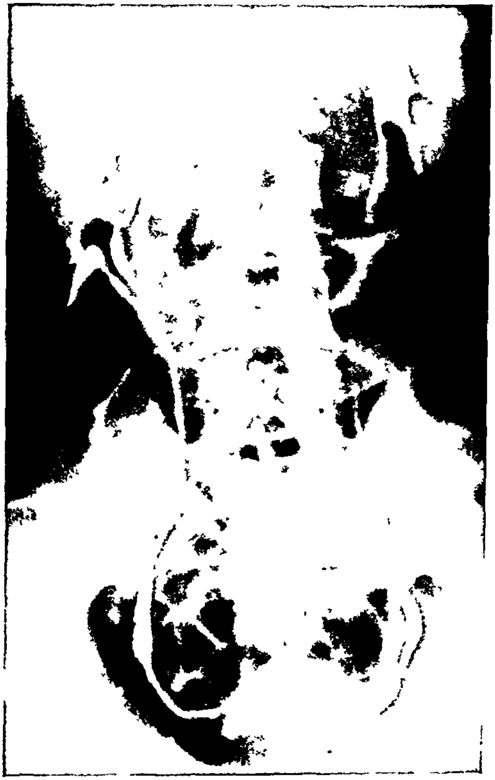

FIG. 3. Retrograde pyelogram showing bifid renal pelvis and filling defect in lower right ureter.

Past history and system review were noncontributory. Physical findings were within normal limits.

Laboratory findings: Complete blood count, normal. Urinalysis, pH 7.0; albumin 0; sugar, 0; acetone, 0; microscopic, many red blood cells and few white blood cells per high powered field. Urea nitrogen, 31.0 mg. per cent; sugar, 108 mg. per cent; calcium, 11.1 mg. per cent; phosphorus, 2.8 mg. per cent; serology, negative.

Cystoscopic observations revealed only moderate prostatic enlargement. Catheters were passed easily to each kidney. Red blood cells were present in both kidney specimens. Pyelograms showed a right bifid renal pelvis as well as a small filling defect in the lower third of that ureter (fig. 3). The hematuria subsided shortly after admission, and the patient was discharged on the sixth hospital day. The discharge diagnosis was "probable right lower ureteral calculus, with possible right ureteral tumor."

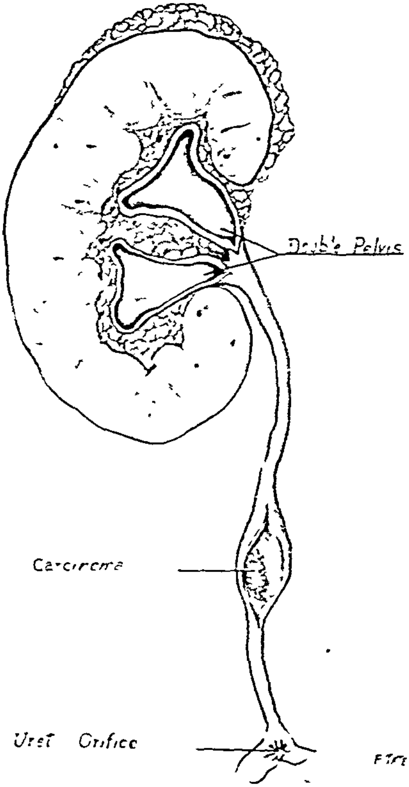

FIG. 4. Drawing of gross specimen, case 2. Note bifid renal pelvis and tumor in lower ureter.

One month afrer discharge, there was a recurrence of hematuria, urgency, frequency and dysuria, and patient was re-admitted. Physical examination was negative and the laboratory findings were unchanged. On cystoscopy, blood was seen coming from the right ureteral orifice but, on passing a catheter up on that side, urine from the upper ureter and pelvis were free of blood. With this finding, a tumor was considered most likely, and exploration was performed. Eight centimeters from the bladder a small, firm, raised, tumor was found. A nephro-ureterectomy with excision of a cuff of the bladder was performed without difficulty.

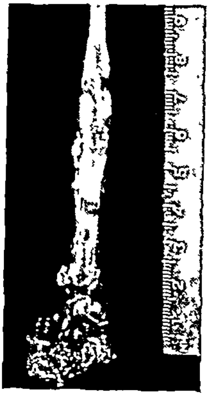

Fig. 5. Photograph of tumor in case 2 showing cuff of bladder at one end

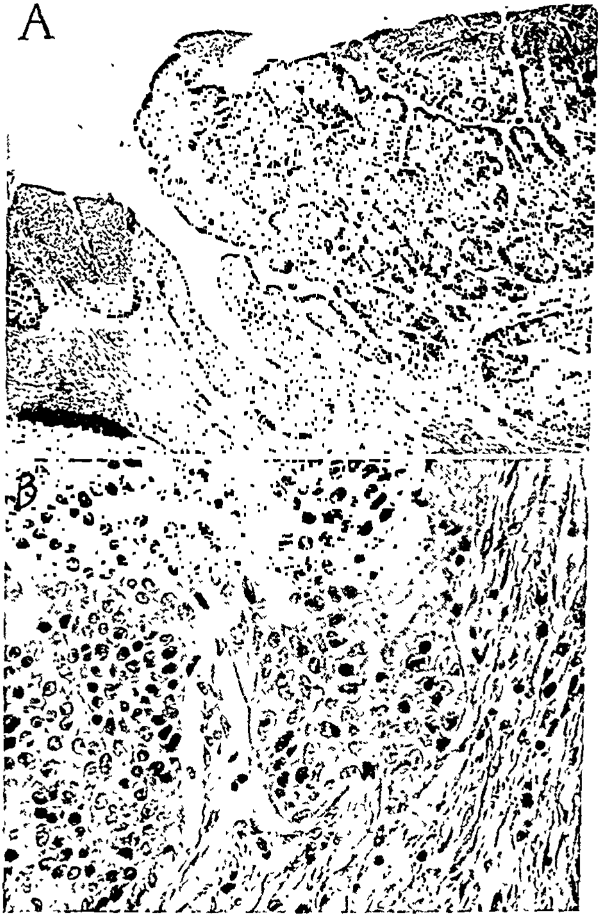

Fig. 6. *A*, papillary transitional cell carcinoma of ureter. Tumor present at free surface and is seen invading submucosa. *B*, high power view of *A*. Note aplasia of cells with variation in nuclear size and staining.

Figure 4 shows a drawing of the kidney with the tumor in the lower ureter. Figure 5 is a photograph of the tumor.

The pathological report was as follows: "The ureteral lesion presents an elevated papillary surface covered by an aplastic transitional epithelium (fig. 6, A). These epithelial cells form nests which invade the sub-mucosa. The tumor cells show round or ovoid hyperchromic nuclei with one or more prominent nucleoli. Mitoses average one per high power field (fig. 6, *B*). . . . The muscularis shows scattered collections of lymphocytes, but no invasion by tumor . . . the kidney shows well-preserved cortex, medulla, and pelvis. . . . Diagnosis: Papillary transitional cell carcinoma of the ureter. grade 3." The follow-up report of this patient is short, 6 months, but in this time there is no evidence of any recurrence of the tumor.

TABLE 1

TUMOR TYPES	NUMBER OF CASES	PER CENT
1. Papillary carcinoma	56	42.4
2. Benign papilloma	26	19.7
3. Transitional cell carcinoma	20	15.0
4. Squamous cell carcinoma	9	6.8
5. Epithelioma	4	3.0
6. Papillary epithelioma	2	1.5
7. Epidermoid carcinoma	2	1.5
8. Adenocarcinoma	2	1.5
9. Papillary fibro-epithelioma	2	1.5
10. Hemangioma	2	1.5
11. Alveolo-papillary carcinoma	1	0.8
12, Benign fibro mucous polyp	1	0.8
13. Sarcoma	1	0.8
14. Scirrhous carcinoma	1	0.8
15. Leiomyosarcoma	1	0.8
16. Benign papilloma transitional	1	0.8
17. Fibroma	1	0.8
Total	132*	100 0

* Two bilateral cases

THE CLINICAL AND DIAGNOSTIC FACTORS IN CARCINOMA OF THE URETER

Tumor types. The incidence of tumors in the urinary tract, as given by Douglass, is 86.5 per cent for the bladder and renal cortex, while only 8.4 per cent for the ureter and renal pelvis. The types of tumors fall into two main categories, papillary and nonpapillary, with the former predominating. Table 1 lists the 17 different types of primary ureteral tumors described in the 130 cases gleaned by us from the literature since 1943. This compares favorably with Scott's 16, and Lazarus' and Marks' 15 different types of tumors. In our group 64.6 per cent are papillary, and 35.4 per cent are nonpapillary. The first four types of tumors listed form 84 per cent of the total number we found in the literature. These are papillary carcinoma (42.4 per cent), benign papilloma (19.7 per cent), transitional cell carcinoma (15 per cent), and squamous cell carcinoma (6.8 per cent). The remaining 19 cases comprise 16 per cent of the total 130 cases.

Age incidence. The age incidence conforms closely, but not wholly with other investigators. The fifth, sixth and seventh decades of life comprise 80.7 per cent of the cases observed (table 2). The sixth decade is first (41 per cent), agreeing with Lazarus and Marks, but not with Scott who placed the fifth decade first. In our cases the fifth decade was second with 28 per cent, and the seventh decade third with 15 per cent of the 130 cases reviewed. The types of tumors in various age groups are what one would expect. The majority of cases of papillary carcinoma occur in the fifth and sixth decades (40 out of 55 cases). The greatest number of these 40 cases are in the sixth decade by a ratio of 24 to 16 (3:2). In benign papilloma the majority of cases are also in the fifth and sixth decades, but here the ratio is 11 to 11 (1:1). This trend of greatest incidence in the sixth and fifth decades follow in the remaining classes of tumors.

Sex incidence. Ureteral tumors are seen most commonly in men. This was confirmed by our group with 65 per cent male and 35 per cent female. The male led in all categories of tumors except transitional cell carcinoma, and this is not statistically significant.

TABLE 2. *Age incident*

DECADE	MALE	FEMALE	TOTAL	PER CENT
1st				
2nd	2	1	3	2
3rd	1	4	5	4
4th	9	3	12	9
5th	22	13	35	28
6th	37	15	52	41
7th	7	11	18	15
8th	2		2	1
	80	47	127	100
No age			1	
No sex			2	
			130	

Tumor location. The commonest location for a tumor is in the lower third of the right ureter. This is similar to preceding reports; however, there is very little difference of right over left in our analysis (35–33 per cent). There is little question that the lower third of both ureters is the commonest site of origin (67 per cent). Ascending the ureter the incidence decreases proportionately. Two of our cases reported the entire right ureter as being involved.

Symptomatology. One of the most significant and appalling points in our analysis of 130 cases was the length of time between the onset of symptoms and the diagnosis and treatment of the tumor. An average lapse of time before diagnosis of 25.1 months for tumors on the right side, and 16 2 months for tumors on the left side was found. The over-all time was more than one and one-half years (20.65 months). It is with these facts in mind that we hope to be able to show the need for more vigorous action, so that less time is lost before diagnosis and treatment are instituted.

A triad of symptoms exists consisting of hematuria, pain and abdominal mass. These are listed in the order of frequency. Hematuria is present in only 70 per cent of the cases found in the literature to date; however, it is present in 92 per cent of our series of 130 cases. Pain is found in over 50 per cent, and abdominal mass is less than 20 per cent. The complete triad is seen 86 per cent of the time in tumors on the right side, and 76 per cent in tumors on the left side. The 10 per cent difference is to be expected since there are more tumors on the right side.

Associated symptoms seen at times are urgency, frequency, dysuria, long slender blood clots, nocturia, weight loss, anorexia, nausea, vomiting, jaundice, right-sided varicocele, chills and fever.

Diagnosis. Cystoscopy and retrograde pyelograms are indispensible in the preoperative diagnosis of ureteral tumor. This is evident in our series where the tumor is seen protruding into the bladder in only 16 per cent of the cases. In this same group of 130 cases, complete obstruction to ureteral catheterization is met in 56 per cent, and incomplete obstruction in 3 per cent. This shows that in 74 per cent of the cases, some local pathological change is evident at the time of cystoscopy. In reviewing these cases it is impossible to determine the number of cases that have no urinary excretion, or bleeding from a ureteral orifice, at the time of cystoscopy.

Roentgenography. Careful study of the 130 cases in our series fails to discover definitely the value of x-ray diagnosis. Generally speaking, x-ray evidence was usually strong enough to warrant a tentative diagnosis which led to exploration. These 130 cases were all definite tumors, and any statistics to show missed cases would be impossible. With the exception of those cases where the tumor is seen, or where unilateral hematuria is evident, x-ray evidence must be depended upon.

The commonest x-ray picture is one of ureteral obstruction, and is seen as a narrowing or filling defect, with ureteral dilatation above and often below the area in question. Figure 3 reveals (case 2) a filling defect in the lower third of the right ureter. The distal ureteral dilatation is explained by Grossman and Allyn as a mechanical blockage by the tumor due to peristaltic action causing it to descend and ball-valve the ureter. The infiltrating tumors usually cause an irregular diminution of the caliber of the ureter with only proximal dilatation. The papillary tumors, solid or pedunculated, may show a goblet-shaped filling defect with dilatation above and below the lesion.

Whenever complete ureteral catheter obstruction is met, it is advisable to place the patient in the Trendelenburg position, and try a Woodruff catheter in the ureteral orifice, for complete ureterograms. Frequently one is able to get enough dye past the obstruction to permit outlining a ureteral defect, with proximal dilatation. In cases where there is no hydro-ureter, or mechanical obstruction to indicate the presence of pathological change, it is our belief that many cases are missed through neglect. The Woodruff procedure is particularly valuable since ureterograms taken with conventional ureteral catheters often do not show the entire distal ureter. Suspected cases should have complete ureterograms in order to discover early lesions. Where hydro-ureter is present, even the most careless pyelography usually shows disease since the dye diffuses well. When no disease is seen with hydro-ureter, the urologist realizes the necessity for a Woodruff study. It is in those cases without ureterectasis, that one is apt to ignore an early or even advanced tumor. This is a cardinal indication for a Woodruff study.

Excretory urograms are usually of little value in establishing a diagnosis. They may show a nonfunctioning kidney when complete obstruction finally occurs. Plain roentgenograms may be of help also in the demonstration of an enlarged kidney, or show metastases to the bones or lungs.

Therapy. Despite the fact that most urologists agree on the treatment of primary malignant ureteral tumors, table 3 shows 15 forms of therapy. This may be partially explained because of the following factors: 1) the general condition of the patient; 2) the functioning quality of the opposite kidney; 3) the location and extent of the tumor locally and distantly; 4) the mechanical difficulty encountered at the time of operation. It is agreed that nephro-ureterectomy with partial cystectomy (cuff of the bladder) is the operation of choice whenever possible for malignant tumors. Some authors believe all ureteral tumors are potentially malignant, and therefore should be treated as such. Vest has an excellent article on the local excision of benign ureteral tumors. He has an elaborate method for establishing the diagnosis of these tumors, at the time of operation. He presents 3 cases with 7½ years, 2½ years, and 3⅓ years' survival, treated with local resection with end-to-end anastomosis. It is conceivable that this may be done safely in a few cases, but it would be difficult for most people

TABLE 3. *Therapy*

TYPE OF PROCEDURE	TOTAL CASES
1. Nephro-ureterectomy with partial cystectomy One stage 20 Two stage 10.	30
2. Nephro-ureterectomy (complete) One stage 45 Two stage 10	55
3. Nephro-ureterectomy (partial)	12
4. Local excision with end-to-end anastomosis, or re-implantation into the bladder	12
5. Nephro-ureterectomy followed by x-ray therapy	4
6. Nephrectomy with partial ureterectomy and fulguration of stump.	3
7. Nephro-ureterectomy with partial cystectomy followed by x-ray therapy	2
8. Roentgen therapy followed by nephro-ureterectomy	2
9. Nephro-ureterectomy, fulguration and x-ray therapy	1
10. Ureterectomy	1
11. Cautery	1
12. Cautery with partial ureterectomy	1
13 Fulguration followed by nephro-ureterectomy (partial)	1
14. Cystectomy with bilateral partial ureterectomy with ureteral cutaneous transplants	1
15. Roentgen therapy (died preoperatively)	1
16. Post-mortem	2
17. No therapy listed	1
Total	130

with less trenchant minds. This was demonstrated in two of our "so-called benign" cases, in which the patients died within 1 to 2 years of metastases.

In our 130 cases analyzed, a greater number of nephro-ureterectomies are found than nephro-ureterectomy and partial cystectomy (55 as to 30). (See table 3.) This may be explained by the foregoing factors, and also by lack of adequate understanding of the problem. A few cases (Douglass) had partial ureterectomy with nephrectomy. Treatment here was usually influenced by one of the aforementioned contra-indications to extensive surgery. Local excision and re-anastomosis by end to end methods was used in 12 cases, both benign and malignant. There was a poor follow-up of these cases so that it was impossible to evaluate them adequately. The majority of remaining surgical methods listed have been used to fit a particular situation. There has been very little benefit derived from the pre- and postoperative use of x-ray therapy, and for this reason it has not been generally adopted. Fulguration in connection with other methods of treatment is listed; however, this form of therapy should not be substituted for excision of a cuff of the bladder. Fulguration alone is of very little value in the curing of this disease, as was demonstrated in our first case report.

TABLE 4. *Follow-up*

TIME SINCE OPERATION	RECURRENCES FOUND IN:								DEATH FROM OTHER CAUSES	MISCELLANEOUS
	Bladder	Ureter	Local recurrence	Lung	Bone	Brain	Carcinomatosis	None found		
1–6 mos.	3	2	1	1			3	14		
6–12 mos.	1	2	2	1	1		4	11	3	
12–18 mos.	1				1			2		
18–24 mos.	2					1	1	7		
2–3 yrs.			1	1				5		
3–4 yrs.	1						1	6	1	
4–5 yrs.	2							1		
5–6 yrs.								1		
6–7 yrs.								3		
7–8 yrs.	1							2		
8–9 yrs.	1	1	1	1			1			

Death on the table	1
Preoperative death	1
Postoperative death (1 day)	1
Total number of cases reporting follow-up	83 (63.9%)
Total number of cases without follow-up	47 (36.1%)
Total	130 (100%)
Average length of time for follow-up (months)	23.2

Follow-up studies. The follow-up studies in the literature are poor in contrast to the thoroughness of diagnosis and therapy. Table 4 reveals 47 cases without follow-up studies. Crance and Knickerbocker report a 25 year survival, and Scott

TABLE 5. *Causes of death*

TYPE OF TUMOR	DURATION SINCE DIAGNOSIS	CAUSES OF DEATH	TYPE OF THERAPY
1. Epithelioma	20 mos.	Metastasis—brain—lung	N.U.B.
2. Epithelioma	5 mos.	Unknown	N.U. (Part.)
3. Papillary carcinoma	12 mos.	Carcinomatosis	N.U.B.
4. Papillary transitional cell carcinoma	6 mos.	Carcinomatosis	N.U.B.
5. Squamous cell carcinoma.	2 mos.	Carcinomatosis	N.U.
6. Papillary squamous cell carcinoma	12 mos.	Metastasis wound, bone	N.U.
7. Sarcoma		Unknown (carcinomatous)	None
8. Squamous cell carcinoma..	7 mos.	Carcinomatosis	N.U. (X)
9. Papillary transitional cell carcinoma	96 mos.	Carcinomatosis	1. Segmental 2. N.
10. Papillary transitional cell carcinoma	10 mos.	Carcinomatosis	1. Ful. 2. N.U. (Part)
11. Leiomyosarcoma	24 mos.	Carcinomatosis (found at P.M.)	None
12. Papillary squamous cell carcinoma	36 mos.	Carcinomatosis	N.U.
13. Transitional cell carcinoma	12 mos.	Carcinomatosis	N.U. (X)
14. Papillary carcinoma	12 mos.	Unkown	N.U. (Part.)
15. Transitional cell carcinoma	Pre-op.	Carcinomatosis	None
16. Alveolo-papillary carcinoma	10 mos.	Pulmonary embolus	N.U.B. (X)
17. Papillary carcinoma	16 mos.	Carcinomatosis	N.U.B. (X)
18. Epidermoid carcinoma	60 mos.	C.V.A.	N.U. (Part.)
19. Epidermoid carcinoma	8 mos	Carcinomatosis	N.U.
20. Transitional cell carcinoma	1 day	Postoperative	N.U.B.
21. Transitional cell carcinoma	54 mos.	Bladder	N.U.B.
22. Papillary carcinoma	12 mos.	Postoperative thyroidectomy	N.U B.
23. Squamous cell carcinoma.	8 mos.	Uremia	N.U. (X)
24. Transitional cell carcinoma		Operative	N.U.B.
25.			

Average survival for all tumors	21.1 mos.
Average survival papillary carcinoma	26.85 mos.
Average survival infiltrative forms	16.11 mos.

Key to "Type of Therapy"

1. N.U.B. Nephro-ureterectomy and partial cystectomy.
2. N.U.B. (X) Nephro-ureterectomy and partial cystectomy with x-ray therapy.
3. N.U. Nephro-ureterectomy (complete).
4. N U. (Part.) Nephro-ureterectomy (partial)
5. N.U. (X) Nephro-ureterectomy with x-ray therapy.
6. Segmental resection of ureter.
   N. Nephrectomy.
7. Ful. Fulguration
8. None No therapy

TABLE 5.—*Continued*

TYPE OF THERAPY	NUMBER OF CASES	AVERAGE SURVIVAL MONTHS
1. N.U.B.	7	20.8 (for 5 cases)
2. N.U.	4	14.5
3. N.U. (Part.)	3	25.66
4. N.U.B. (X)	2	13.0
5. N.U. (X)	3	9.0
6. Ful. and N.U.	1	10.0
7. Segemntal and N.	1	96.0
8. Preop.	1	0.0
9. None	2	0.0

lists a 10 year survival in previously reported cases. In our analysis of 130 cases the best survival time was 9 years. In 52 of our cases without recurrence, 2 patients were seen for 8 years; however, 50 per cent of these 52 cases were only seen for a year or less. (See table 4.)

The number of cases with a follow-up is small, and therefore no definite statements may be made. However, we do see that the commonest site of recurrence is in the bladder, the ureter, the peri-ureteral structures, the lung, the bone, and the brain, in the order listed. Carcinomatosis was the commonest cause of death. Table 5 reveals the causes of death in 24 cases compared with the types of tumors, their survival time, and type of therapy used. The longest survival was for 8 years. The average survival time, with the exclusion of the operative mortality and the one unknown case, was 21.1 months. This is 5 months shorter than the papillary forms, and 5 months longer than in the infiltrated forms. This indicates that the infiltrated forms are more highly malignant than the papillary tumors. This is explained in the fact that the infiltrative tumors metastasize more readily. The normally thin ureteral wall lends itself more readily to invasion, and hence to blood and lymphatic vessels infiltration. The comparison of the survival time to the type of therapy given is too small in number to be of significance. (See table 5.) However, it is interesting to note that nephro-ureterectomy with partial cystectomy has a longer survival than does just nephro-ureterectomy.

DISCUSSION

Primary carcinoma of the ureter is no longer the rarity it was once considered, but rather is more often diagnosed in time so that therapy may be instituted. However, there is still a need for improvement in the early diagnosis of this condition. With today's facilities at hand: Papanicoloau staining of the urinary sediment, cystoscopy, and roentgenological examination, there is no reason that the average 20.6 months that exists before diagnosis in our series cannot be shortened. Carcinoma of the ureter is an insidious disease, but one that affords relatively easy diagnosis, and therefore an opportunity for a proper solution. Greater alertness on the part of the medical profession to minor urinary complaints, hematuria, pain, and an abdominal mass, would decrease the delays in diagnosis.

The order of frequency in which the tumors appear is similar to previous reports: papillary carcinoma (42.4 per cent), benign papilloma (19.7 per cent), transitional cell carcinoma (15 per cent) and squamous cell carcinoma (6.8 per cent). The tumor is seen most frequently in the male during the sixth decade of life. Previous reports found the right ureter involved most often; however, in our group there was an insignificant difference of the right over the left (35–33 per cent).

Hematuria was found more frequently than previous reports indicate (70 to 92 per cent). This is mainly gross hematuria, but occasionally it is only microscopic. The presence of hematuria warrants cystoscopy, and if during this procedure no foci of bleeding are evident, careful ureterograms are indicated. If improper filling of the ureters is present in the routine procedure, Woodruff ureterograms should be performed. It is believed if this latter method is done in obscure cases, a great many more ureteral tumors would be discovered, and seen at an earlier date. The other main symptoms of flank or abdominal pain and an abdominal mass, are not wholly suggestive of tumors by themselves, but in the presence of hematuria are suggestive of tumor.

A great variety of treatments are seen (table 3), but the generally accepted method of choice for malignant ureteral tumors is nephro-urecterectomy with partial cystectomy. It is frequently stated that all ureteral tumors are potentially malignant, and therefore, should be handled in the most radical manner practicable.

It is quite conceivable that benign tumors are found in the ureter; the only factor is the ability to recognize them promptly and correctly at the time of operation. Vest has presented a fine paper describing the manner and proper approach to this subject. One of the poorest aspects of the picture of ureteral tumors is the follow-up. In our 130 cases analyzed there were only 83 cases followed up. There was no longer than a nine year follow-up with an average of two and a sixth year follow-up. The great majority had less than one year follow-up.

As it stands today, the average survival in our small series of 24 cases is 21.1 months. Papillary carcinoma survival was 5 months better than this, while the infiltrative forms proved more highly malignant with 5 months less survival than the average for all tumors. It is hoped that the surgeons who have written previous reports on this subject will make a follow-up study so that we may properly reevaluate the ureteral tumor situation.

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SUMMARY

Since 1943, one hundred and twenty-eight cases have been found in the literature and 2 new cases have been added. Total number of cases as of May 1951 is 310.

Figures concerning the tumors generally agree with previous studies.

Striking points of interest are: 1) A lapse exists of 20.6 months before diagnosis is made. 2) Nephro-ureterectomy with partial cystectomy, whenever possible, is the therapy of choice for malignant tumors. 3) Only 63 per cent of the cases had a follow-up, and that was for 2⅙ years. 4) Survival for 20 cases was 21.1 months.

Suggestions: 1) increased cancer consciousness of the public; 2) increased consciousness for ureteral tumors by the urologist; 3) better use of diagnostic implements; 4) more radical surgery whenever possible.

Since the writing of the paper, it has been brought to our attention that Dr. J. A. Campbell Colston has a case of ureteral tumor previously reported in the *Journal of Urology* (1935) with a 14 year survival. This patient died without evidence of any recurrence.

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ANTICHOLINERGIC (BANTHINE) INFLUENCES ON NORMAL AND NEUROGENIC BLADDER FUNCTION

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Urinary frequency and incontinence complicating the management of the neurogenic bladder are often distressing problems to both patient and physician. In selected cases, banthine, because of its powerful and prolonged parasympathetic blocking action, offers promise for the control of this condition.

The concept of urinary control by a medicinal agent capable of inhibiting a spactic detrusor muscle is not new. Langworthy[1] (1936) found atropine to be of value in relieving urgency and frequency of urination in patients with spastic paraplegia. Bladder capacity was increased from 150 cc to 250 cc and urinary frequency was reduced. However, atropine sulfate had to be gradually increased to the limits of tolerance with the consequent development of distressing side reactions. Since Langworthy's initial attack on the problem, little has been contributed which would substantiate the potentialities of atropine or other parasympathetic blocking agents in the management of the spastic urinary bladder. In the light of present theories regarding neurogenic bladder dysfunction and the availability of a new, more potent anticholinergic drug, the following investigational study was carried out.

PHYSIOLOGY OF THE NORMAL BLADDER

A short résumé of normal bladder physiology is fundamental to an understanding of neurogenic bladder dysfunction and the selection of appropriate cases for drug therapy. For the purpose of this discussion, bladder activity can be considered to be dependent upon three levels of control. Starting with the basic inherent properties of smooth muscle, there is progression of complexity evident. The isolated bladder will demonstrate tonus and accommodation to filling, but a coordinated expulsive contraction is impossible, due to the lack of an integrating mechanism. Clinically, such bladder behavior is noted in the state of "spinal shock" following cord injuries, as demonstrated by Nesbit and Lapides.[2] Likewise, spinal anesthesia removes central nervous system integration with resulting temporary urinary retention. The second level of control becomes apparent with the addition of a reflex arc mediated through sacral cord segments 2, 3, 4. The forceful involuntary expulsion of urine can now occur, but the volume and frequency will depend upon the threshold of reflex activity. Residual urine is the rule and superimposed infection may lower the threshold stimulus to such an extent that adequate filling becomes impossible. Yet a third level of complexity acts to

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[1] Langworthy, O. R.: A new approach to the diagnosis and treatment of disorders of micturition in diseases of the nervous system. Internat. Clin., 3: 98, 1936.

[2] Nesbit, R. M. and Lapides, J.: Tonus of bladder during spinal "shock". Arch. Surg., 56: 138, 1948.

modify the behavior of the normal adult bladder. This control is an inhibitory influence, originating in cerebral centers, which controls bladder filling by delaying the motor discharge of the spinal reflex arc. The development of this suprasegmental inhibition serves to differentiate the infant from the adult bladder. Normal bladder function depends on the harmonious interplay of a complex series of nervous system controls. Perfect integration at each level is essential as evidenced by the multitude of lesions seen clinically which are known to produce abnormal bladder behavior. Although the foregoing discussion has consisted of generalities, its practicability becomes apparent when applied to the problem of neurogenic bladder dysfunction.

PHYSIOLOGY OF THE NEUROGENIC BLADDER

Five groups (Nesbit[3]) suffice to classify the abnormalities of neurogenic bladder activity. The *uninhibited neurogenic bladder*, group 1, results from failure to develop or acquired loss of the suprasegmental inhibitory center. Frequency, urgency and enuresis are prominent symptoms; precipitous evacuation without residuum, associated with the findings of small bladder capacity and intact sensation, complete the diagnostic criteria of this group. Acquired lesions such as cerebral vascular accidents, brain tumors and prefrontal lobotomy are etiologic lesions in producing uninhibited neurogenic dysfunction.

Group 2 has been termed the *reflex neurogenic bladder*. This condition results from complete transection of the spinal cord or comparable lesions above the level of the conus medularis. Periodic involuntary voiding occurs, but bladder sensation is absent. A residual urine of one or more ounces predisposes to urinary sepsis.

With interruption of both afferent and efferent peripheral nerve pathways to the bladder, group 3, the *autonomous neurogenic bladder*, results. Sensation, reflex micturition, and voluntary control are all lost, with remaining function consisting solely of the inherent properties of smooth muscle. Tonus and accommodation to filling remain; there is emptying of the distended viscus by overflow incontinence.

The *sensory paralytic bladder*, group 4, is exhibited in those cases in which bladder sensation is selectively abolished. The dorsal root lesions of tabes dorsalis effectively interrupt these afferent pathways. Filling and evacuation can proceed in a normal manner. However, the stimulus for voiding never reaches the spinal or cerebral levels, and eventually chronic overfilling will produce a decompensated reservoir. Detrusor power is destroyed by unperceived chronic overdistension.

Lastly, the *motor paralytic bladders* may be considered as group 5. Painful distension occurs, but voluntary or reflex expulsion of urine cannot take place. The detrusor is at the mercy of its contents with overflow, decompensation, and atonicity being the chain of events.

In the latter three groups, normal detrusor tonus prevails until the time when decompensation and atonicity supervene. With groups 1 and 2, the situation is the reverse. Hyperactivity of the detrusor muscle manifests itself as urinary frequency and is the source of the afflicted patient's complaints. With these thoughts in mind, the pharmacology of banthine will suggest at once the clinical application of this drug.

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[3] Nesbit, R. M.: Fundamentals of Urology. 3rd Ed. 1949.

PHARMACOLOGY OF BANTHINE

The pharmacology of banthine (beta-diethylaminoethyl xanthene-9-carboxylate methobromide) has been reported by several groups of investigators since its introduction in 1949. Most studies have been directed toward control of gastric motility and secretion, the effects on the urinary bladder being considered as undesirable side reactions. The action of banthine is that of a long acting anticholinergic agent. Nerve impulses of the parasympathetic system are blocked at the ganglia and at the effector sites. Since acetylcholine is the chemical mediator for neural transmission across sympathetic ganglia, some inhibition occurs also on the sympathetic side. The inhibition of parasympathetic activity would appear to be the stronger of the two nervous system blockades.

Detrusor activity depends upon parasympathetic innervation. Hambourger et al.[4] reported the effect of anticholinergic agents on the pressure changes which occur in the dog's bladder when standardized repetitive electrical stimuli are applied to the pelvic nerve. The intravenous injection of either banthine or tetraethylammonium chloride completely abolished the standardized response. When compared with TEAC, banthine proved twice as effective, weight for weight.

METHODS

The clinical material for this investigation consisted of four normal subjects plus fourteen patients with neurogenic bladder dysfunction. The latter cases are further classified on the basis of their cystometrographic features (table 1).

A Lewis continuous recording cystometer was used to record the changes in intravesical pressure before and after the administration of banthine. Comparable curves were obtained on repeated measurements of normal and of neurogenic bladder states.

Procedure. The presence or absence of residual urine is determined. A 20F catheter is used since a large caliber lumen facilitates a more rapid equilization of pressure changes. This catheter is connected to the cystometer, which, in turn, is joined by a suitable length of rubber tubing with a 1,000 ml. graduated flask, placed four feet above the level of the symphysis pubis. A drip chamber interposed between the flask and cystometer makes it possible to regulate the flow of sterile saline solution at approximately 50 cc per minute. The arrow provided on the front of the cystometer must be level with the symphysis pubis.

We have found it desirable to record continuously rather than by increments in order to more closely portray the entire intravesical sequence. As the bladder slowly distends, the patient is instructed to indicate the first desire to void (*), the sensation of filling (F), and the onset of painful distension (P). These particular symbols, originated by Rose, have been adopted by us in order to facilitate comparison of our studies with those of other investigators. These points along the pressure curve are carefully recorded, to be utilized in the final interpretation of the record. When distension becomes unbearable, the patient is instructed to void with maximal effort (M), following which the apparatus is quickly disconnected and the bladder contents emptied. The measured volume constitutes the total bladder capacity and provides a check against the quantity of fluid used to distend the bladder as indicated by the cystometrogram. Minor variations in the rate of flow of the irrigating fluid will result in tracings which require the measured bladder capacity for interpretation. Additional information is secured by instilling 60 cc of warm water (41C) so that bladder thermal sensation can be evaluated.

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[4] Hambourger, W. E., et al: Pharmacology of B-diethylaminoethyl xanthene-9-carboxylate methobromide (banthine). J. Pharmacol. and Exper. Therap., 99: 245, 1950.

TABLE 1. *Classification of patients and results of banthine therapy*

NO.	PATIENT	AGE	NEUROGENIC BLADDER GROUPING	THERAPY INDICATED BY CYSTOMETROGRAM?	RESULT	
					Frequency	Incontinence
1.	A. G.	44	Uninhibited	Yes	Improved	Improved
2.	R. B.	23	Uninhibited	Yes	Improved	Improved
3.	J. G.	28	Uninhibited	Yes	Improved	Improved
4.	D. F	13	Reflex	Yes	Improved	Improved
5.	H. P.	38	Reflex	Yes	No clinical trial	
6.	C. A.	50	Reflex	Yes	No improvement due to incompetent external sphincter.	
7.	T. C.	66	Autonomous (early)	No	Temporary condition with spontaneous improvement.	
8.	L. S.	36	Autonomous (late)	Yes	No improvement due to incompetent external sphincter.	
9.	F. S.	39	Autonomous (late)	Yes	No clinical trial.	
10.	A. W.	58	Sensory paralytic	No	Contraindicated	
11.	M. C.	50	Motor paralytic	No	Contraindicated	
12.	I. P.	53	Motor paralytic	No	Contraindicated	
13.	D. L.	9	Motor paralytic	No	Contraindicated	
14.	P. P.	27	Motor paralytic	No	Contraindicated	

CYSTOMETRIC STUDIES BEFORE AND AFTER BANTHINE: NORMAL BLADDER

Curve 1, figure 1, shows the pressure changes recorded during the filling of a normal bladder. The first desire to void (*) was recognized with 100 cc of fluid; painful distension (P) occurred with a volume of 350 cc. Maximal voluntary voiding (M) was then attempted, with intravesical pressure rising to 90 mm. of mercury. Banthine bromide, 25 mg., was administered intravenously. In 20 minutes general systemic effects, as evidenced by dry mouth, dilated pupils and increased pulse rate were apparent. A second measurement was then made, curve 2 of figure 1 being obtained. Similar responses were obtained in three other normal human subjects. The following drug effects are worthy of note:

1) The first desire to void was delayed and required approximately 50 cc additional fluid to register at the cerebral level.

2) Bladder distension was increased by 100 cc before comparable pain was noted.

3) Maximal voluntary pressure was of lesser magnitude, a decrease of 30 mm. of mercury being recorded.

4) Following the removal of the urethral catheter, only 230 cc could be voluntarily voided. A 200 cc residual urine was now found in a bladder which a few minutes previously had been capable of complete evacuation.

5) Finally, it is noted that total bladder capacity was increased from 400 cc to 430 cc.

CYSTOMETRIC AND VOIDING CONTROL STUDIES IN NEUROGENIC STATES (REPRESENTATIVE CASES)

Case 1: A. G., a 44 year old Negro, had suffered an extensive "stroke" which resulted in an uninhibited neurogenic bladder and complete urinary incontinence.

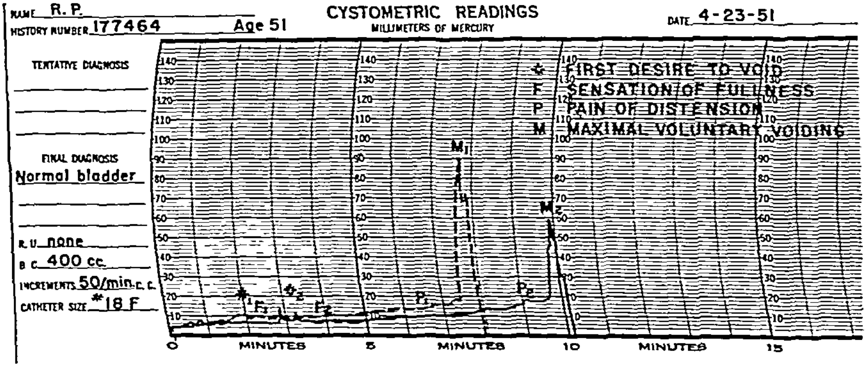

FIG. 1. Cystometric curves recorded during filling of a normal bladder. Curve 1 (broken line) was obtained prior to administration of any drug. Curve 2 (solid line) shows depressant effect of banthine, 25 mg. intravenously, as evidenced by delay in first desire to void (*2), delay in onset of painful distension (P2), decrease in magnitude of voluntary contraction (M2), and increase in bladder capacity.

Mentally, this patient was reduced to a vegetative state, which prevented recording of subjective aspects of the cystometrogram. Curve 1, figure 2, *A*, shows a precipitous type of urination (M_1) with a small bladder capacity of 200 cc. Curve 2, figure 2, *A*, reveals the marked inhibitory effect of a single intravenous dose of banthine, 25 mg. Bladder capacity was increased from 200 cc to 600 cc, (M_1 to M_2), without the occurrence of an effective voiding contraction.

Figure 2, *B* was obtained from the same subject on the following day. Curve O, figure 2, *B* again shows a precipitous voiding contraction with small bladder capacity (125 cc). A single oral dose of banthine, 100 mg., was administered and serial cystometrograms done at hourly intervals. Curves 1, 2, 3 show progressive increase in the degree of detrusor inhibition at 1, 2 and 3 hours following administration with maximal bladder capacity of 275 cc. being reached at 3 hours. At 7 hours (M_7), the inhibitory effect of banthine was still evident, but of lesser degree. These data are presented graphically in figure 3.

comparison of our studies with those of other investigators. These points along the pressure curve are carefully recorded, to be utilized in the final interpretation of the record. When distension becomes unbearable, the patient is instructed to void with maximal effort (M), following which the apparatus is quickly disconnected and the bladder contents emptied. The measured volume constitutes the total bladder capacity and provides a check against the quantity of fluid used to distend the bladder as indicated by the cystometrogram. Minor variations in the rate of flow of the irrigating fluid will result in tracings which require the measured bladder capacity for interpretation. Additional information is secured by instilling 60 cc of warm water (41C) so that bladder thermal sensation can be evaluated.

TABLE 1. *Classification of patients and results of banthine therapy*

NO.	PATIENT	AGE	NEUROGENIC BLADDER GROUPING	THERAPY INDICATED BY CYSTOMETROGRAM?	RESULT	
					Frequency	Incontinence
1.	A. G.	44	Uninhibited	Yes	Improved	Improved
2.	R. B.	23	Uninhibited	Yes	Improved	Improved
3.	J. G.	28	Uninhibited	Yes	Improved	Improved
4.	D. F	13	Reflex	Yes	Improved	Improved
5.	H. P.	38	Reflex	Yes	No clinical trial	
6.	C. A.	50	Reflex	Yes	No improvement due to incompetent external sphincter.	
7.	T. C.	66	Autonomous (early)	No	Temporary condition with spontaneous improvement.	
8.	L. S.	36	Autonomous (late)	Yes	No improvement due to incompetent external sphincter.	
9.	F. S.	39	Autonomous (late)	Yes	No clinical trial.	
10.	A. W.	58	Sensory paralytic	No	Contraindicated	
11.	M. C.	50	Motor paralytic	No	Contraindicated	
12.	I. P.	53	Motor paralytic	No	Contraindicated	
13.	D. L.	9	Motor paralytic	No	Contraindicated	
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CYSTOMETRIC AND VOIDING CONTROL STUDIES IN NEUROGENIC STATES (REPRESENTATIVE CASES)

Case 1: A. G., a 44 year old Negro, had suffered an extensive "stroke" which resulted in an uninhibited neurogenic bladder and complete urinary incontinence.

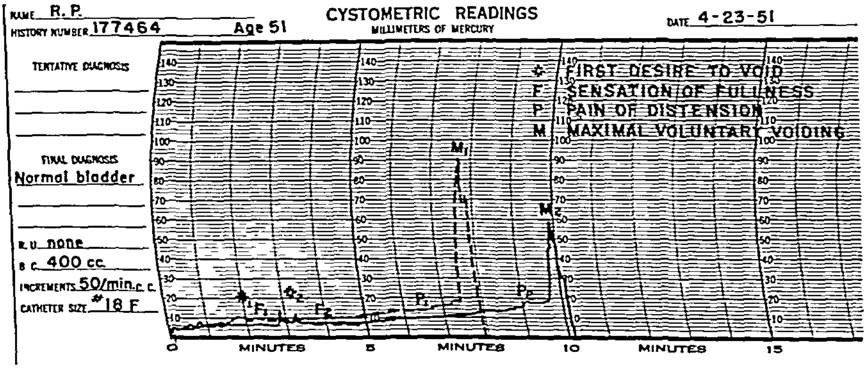
NAME R. P.
HISTORY NUMBER 177464 Age 51
DATE 4-23-51
TENTATIVE DIAGNOSIS
FINAL DIAGNOSIS Normal bladder
R. U. none
B. C. 400 cc.
INCREMENTS 50/min. c. c.
CATHETER SIZE #18 F

FIG. 1. Cystometric curves recorded during filling of a normal bladder. Curve 1 (broken line) was obtained prior to administration of any drug. Curve 2 (solid line) shows depressant effect of banthine, 25 mg. intravenously, as evidenced by delay in first desire to void (*2), delay in onset of painful distension (P2), decrease in magnitude of voluntary contraction (M2), and increase in bladder capacity.

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Figure 2, *B* was obtained from the same subject on the following day. Curve O, figure 2, *B* again shows a precipitous voiding contraction with small bladder capacity (125 cc). A single oral dose of banthine, 100 mg., was administered and serial cystometrograms done at hourly intervals. Curves 1, 2, 3 show progressive increase in the degree of detrusor inhibition at 1, 2 and 3 hours following administration with maximal bladder capacity of 275 cc. being reached at 3 hours. At 7 hours (M_7), the inhibitory effect of banthine was still evident, but of lesser degree. These data are presented graphically in figure 3.

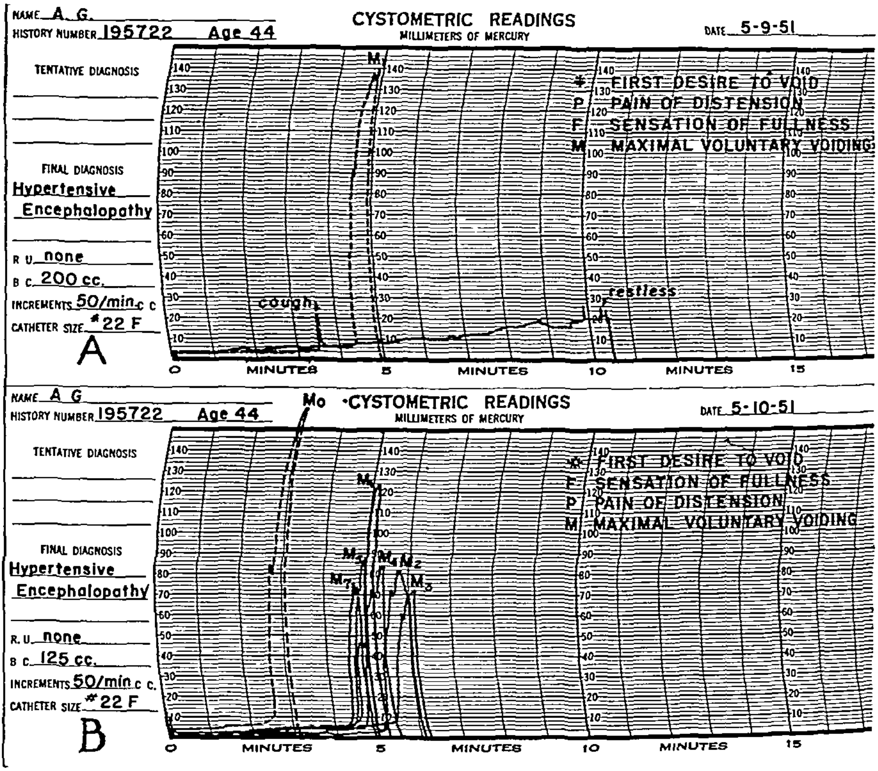


FIG. 2. Case 1. *A*, cystometric study with curve 1 (broken line) showing characteristic precipitous, low volume, involuntary detrusor contraction of an uninhibited neurogenic bladder. Curve 2 (solid line) obtained following banthine, 25 mg. intravenously, indicates blockade of detrusor contractility with resulting increase in bladder capacity. *B*, serial cystometrograms, case 1, evaluating duration of action and time of maximal drug effect following a single oral dose of banthine, 100 mg. Curve 0 (broken line) serves as a base line and was recorded prior to administration of the drug. Curves M1, M2, etc. (solid lines) were subsequently recorded at hourly intervals. See graphic presentation of these data in figure 3.

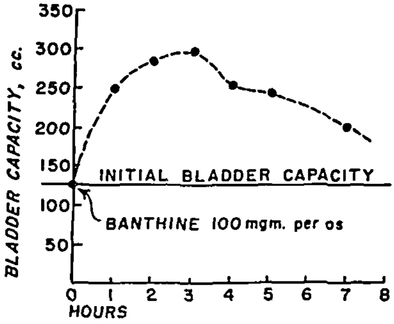


FIG. 3. Graphic presentation of data obtained from serial cystometrograms in case 1, illustrating duration of action and time of maximal depressant effect of banthine on the urinary bladder.

Control of urination. Having demonstrated the remarkable depressant action of banthine on the detrusor muscle in case 1, the next step was to attempt to control frequency of urination. Banthine bromide was started in 50 mg. oral doses, each dose given immediately after urination. No attempt was made to limit the oral intake of fluids during the ensuing 6 day test period. Voiding was initiated by suprapubic pressure applied 5 to 6 hours after the previous voiding. The results are presented in figure 4. With the administration of banthine, the approximate time of urination could be anticipated. Urinary frequency was decreased to three to four times daily with concomitant increase in bladder capacity. Voidings ranging between 350 cc and 400 cc were caught in a urinal after initiating micturition by suprapubic pressure. With discontinuance of the drug, frequency and incontinence recurred. The nursing staff was no longer able to anticipate the time of urination. It was impossible to initiate voiding regularly by suprapubic pressure.

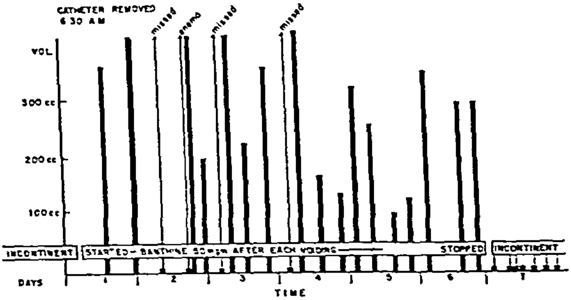


FIG. 4. Control of urinary frequency and incontinence due to uninhibited neurogenic bladder dysfunction (case 1). Banthine inhibition of the detrusor muscle allowed normal bladder filling with resulting decrease in the frequency of urination. Approximate time of voiding became predictable and could be initiated by suprapubic pressure.

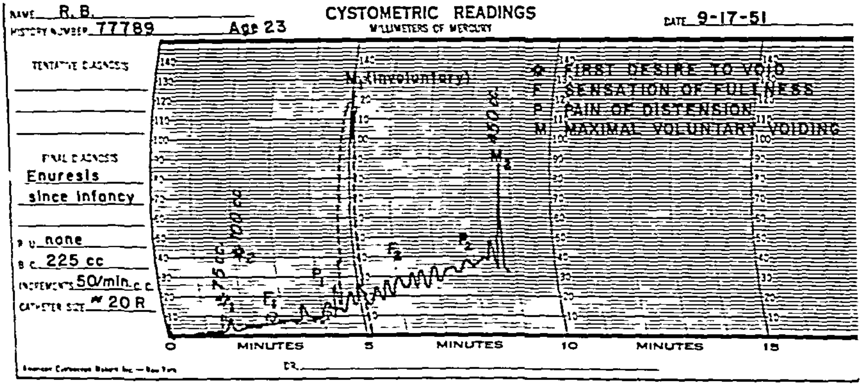
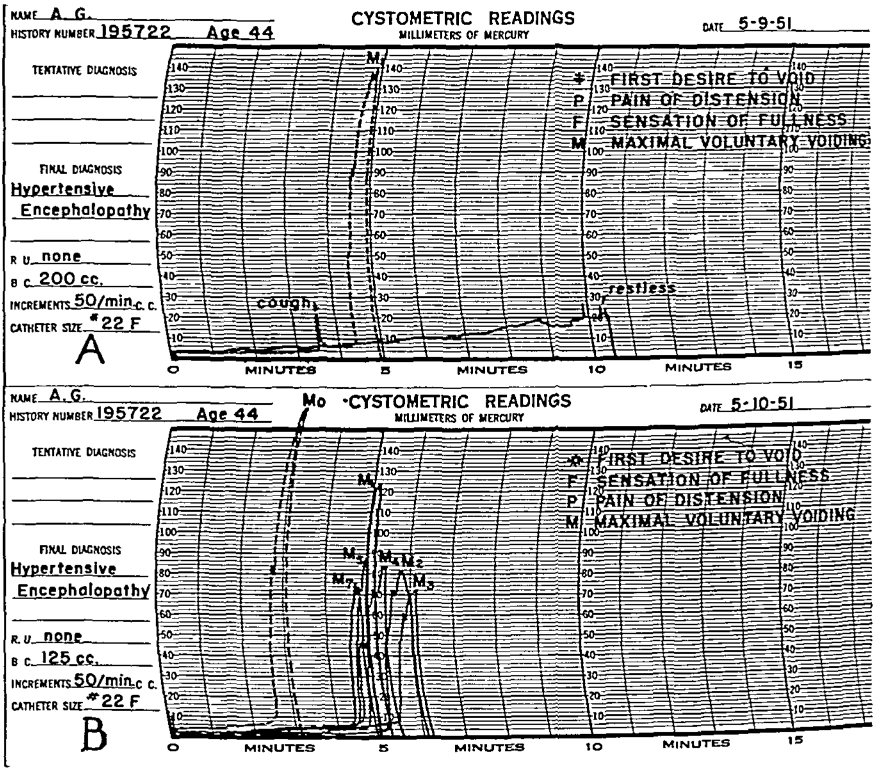

NAME R. B.
HISTORY NUMBER 77789 Age 23
CYSTOMETRIC READINGS
MILLIMETERS OF MERCURY
DATE 9-17-51
TENTATIVE DIAGNOSIS
FINAL DIAGNOSIS Enuresis since infancy
R U none
B C 225 cc
INCREMENTS 50/min. c c
CATHETER SIZE # 20 R

FIG. 5. Curve 1 (broken line) shows an uninhibited neurogenic bladder (case 2) which resulted in frequency, urgency and enuresis. Curve 2 (solid line) was obtained after administration of banthine in 100 mg. oral doses over a three day period. Note marked increase in bladder capacity from 225 cc to 450 cc.

Case 2: R. B., a 23 year old white man, recently had been discharged from military service because of enuresis. Frequency, urgency, and enuresis had been present since infancy. A complete urologic examination, including excretory urograms, cystoscopy, and x-rays of the dorsolumbar spine, failed to provide a clue as to the possible etiology. A cystometrogram, curve 1, figure 5, substantiated



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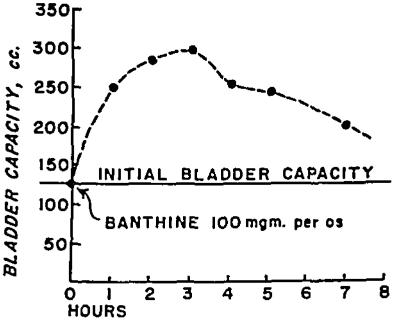

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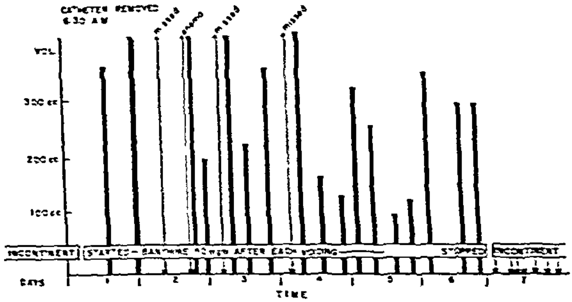

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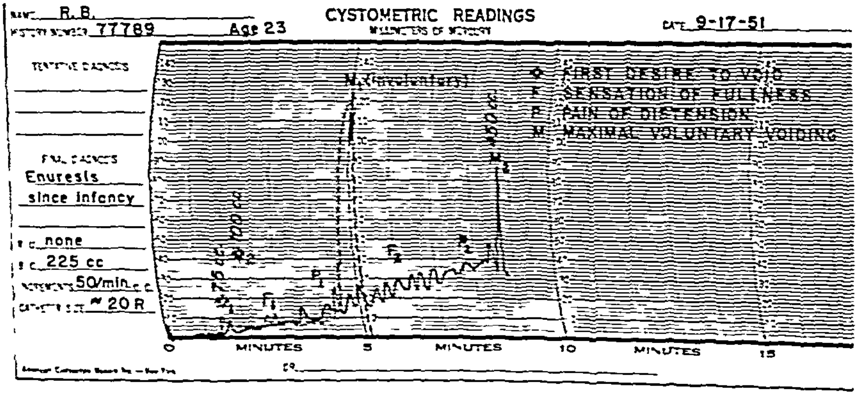
R.B.
77789 Age 23
CYSTOMETRIC READINGS
9-17-51
Enuresis since infancy
none
225 cc
50/min
~ 20 R

FIG. 5 Curve 1 (broken line) shows an uninhibited neurogenic bladder (case 2) which resulted in frequency, urgency and enuresis. Curve 2 (solid line) was obtained after administration of banthine in 100 mg. oral doses over a three day period. Note marked increase in bladder capacity from 225 cc to 450 cc.

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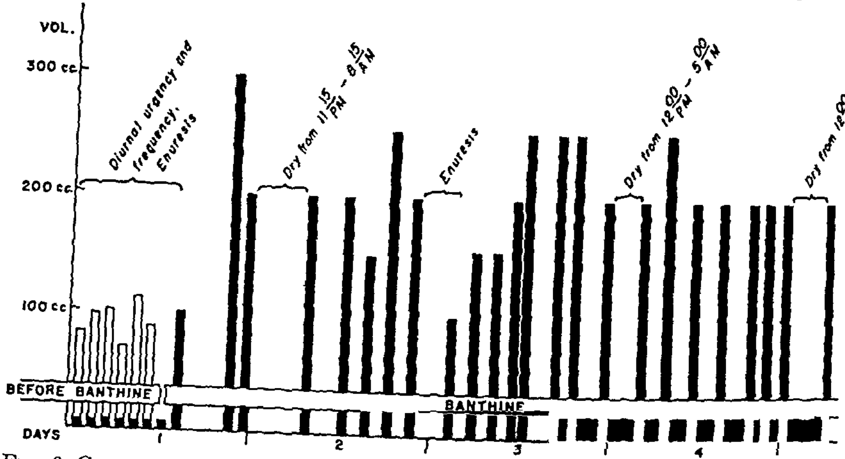

FIG. 6. Control of urinary frequency, urgency and enuresis (case 2) with parasympathetic blockade, banthine 100 mg. orally, every 6 hours. Presenting symptoms were due to an uninhibited neurogenic bladder as evidenced by cystometrogram presented in figure 5.

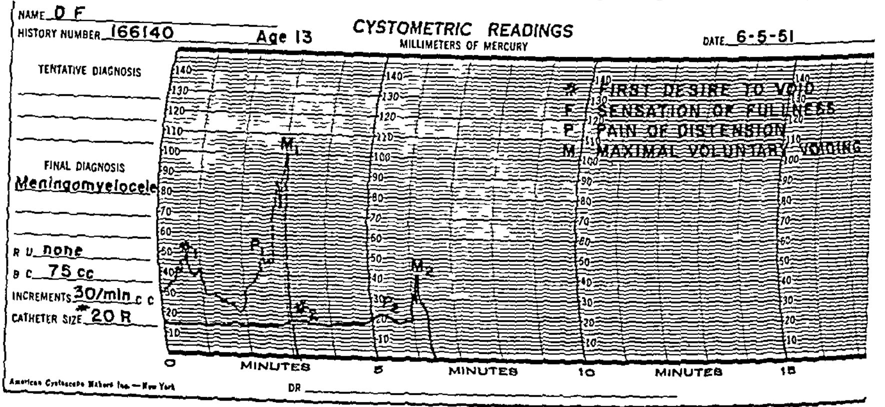
NAME D F
HISTORY NUMBER 166140 Age 13
CYSTOMETRIC READINGS
MILLIMETERS OF MERCURY
DATE 6-5-51
TENTATIVE DIAGNOSIS
FINAL DIAGNOSIS Meningomyelocele
R U none
B C 75 cc
INCREMENTS 30/min c c
CATHETER SIZE #20 R
DR

FIG. 7. Reflex neurogenic bladder (case 4) with hypertonicity and small bladder capacity as shown by curve 1 (broken line). Following administration of banthine, 25 mg. intravenously, desire to void was delayed and bladder capacity was increased from 75 to 250 cc.

The reflex neurogenic bladder is a particularly distressing problem. Case 4, D. F., a 13 year old white boy, exhibited frequency, urgency and incontinence following repair of a meningomyelocele shortly after birth. The cystometrogram, curve 1, figure 7, confirmed the clinical diagnosis of reflex neurogenic bladder.

Curve 2, figure 7, again showed the depressant effect on the detrusor of a single administration of banthine, 25 mg. intravenously, with resulting increase in bladder capacity from 75 cc to 250 cc.

To control frequency and incontinence, banthine, 50 mg. orally, was given after each voiding. The urinary frequency chart (fig. 8) shows graphically the successful management of this problem. Most gratifying was the development of relative continence, with lengthened periods of bladder filling.

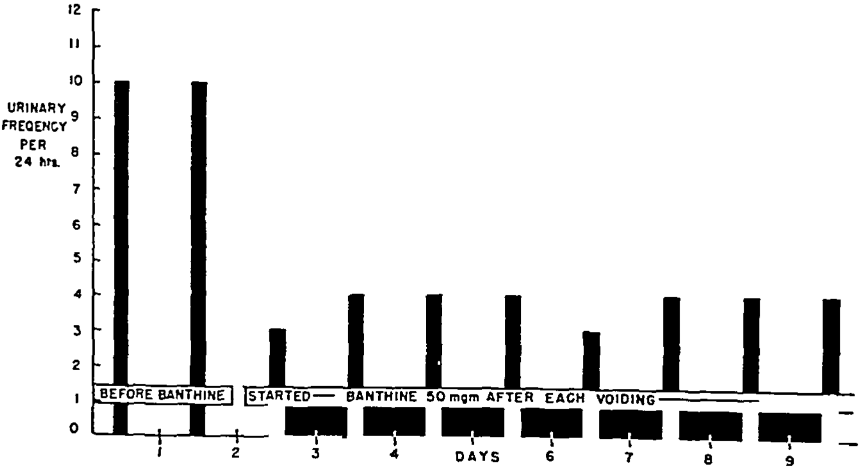

FIG. 8. Clinical study of reflex neurogenic bladder (case 4) with control of urinary frequency by banthine therapy. Frequent, small voidings of 10 times per day decreased to larger volumes of 4 times per 24 hours.

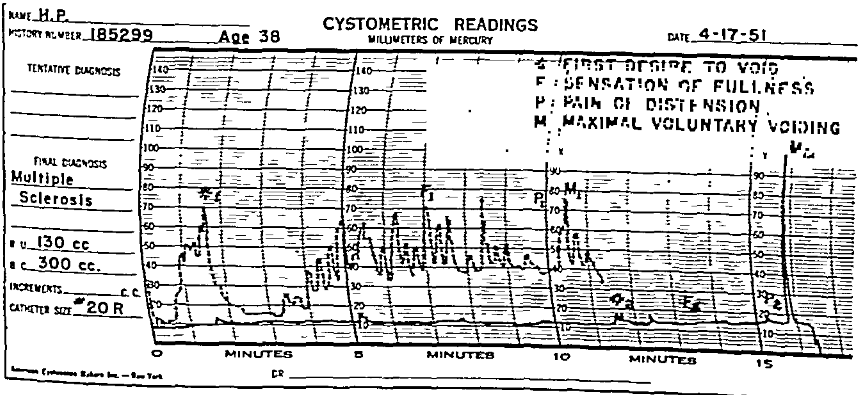
NAME H.P.
HISTORY NUMBER 185299 Age 38
CYSTOMETRIC READINGS
MILLIMETERS OF MERCURY
DATE 4-17-51
TENTATIVE DIAGNOSIS
FINAL DIAGNOSIS Multiple Sclerosis
R U 130 cc
B C 300 cc.
INCREMENTS ____ C.C.
CATHETER SIZE #20 R
DR

FIG. 9. Reflex neurogenic bladder (case 5) with hypertonicity and multiple involuntary contractions appearing in curve 1 (broken line). Banthine effects, demonstrated in curve 2 (solid line) are complete inhibition of spasticity, increase in bladder capacity from 300 cc to 625 cc and delay in first desire to void.

Case 5: H. P., a 38 year old white man with multiple sclerosis, is presented as an example of the inhibitory effects of banthine on a reflex neurogenic bladder. Curve 1, figure 9 shows a hyperirritable bladder with multiple involuntary contractions of the detrusor. Urinary frequency was a prominent symptom since the first desire to void (*) occurred with a volume of only 75 cc. Banthine bromide, 25 mg. intravenously, brought about the marked inhibitory effect shown in curve 2, figure 9, with an increase in bladder capacity from 200 cc to 625 cc.

Case 6: C. A., a 50 year old white woman, having a spinal cord tumor in the lower cervical region, presents a third example of the reflex neurogenic bladder, evidenced by curve 1, figure 10. Here again, involuntary hypertonic detrusor activity was depressed and bladder capacity was increased from 75 cc to 250 cc. However, due to paralysis of the external urethral sphincter, urinary incontinence was not benefited by the use of banthine. Complete loss of sphincter tonus rendered drug therapy ineffective in promoting bladder control.

In the course of this investigation, several absolute contra-indications to banthine therapy became evident. One patient with early prostatism and a residual urine of 50 cc experienced a prolonged exacerbation of symptoms following a single intravenous injection of banthine, 25 mg. The hypotonic bladder states, irrespective of etiology, were further compromised by the parasympathetic blockade; the motor paralytic group is a prime example. Although no patient exhibiting glaucoma, myasthenia gravis, or severe cardiac disease was encountered, theoretical considerations would indicate that banthine might be dangerous. A relative contra-indication exists in the presence of a completely incompetent sphincter mechanism. No harmful effects were noted, but incontinence and frequency were not improved. The mild constipation associated with continued use of the drug was relieved by use of appropriate mild laxatives.

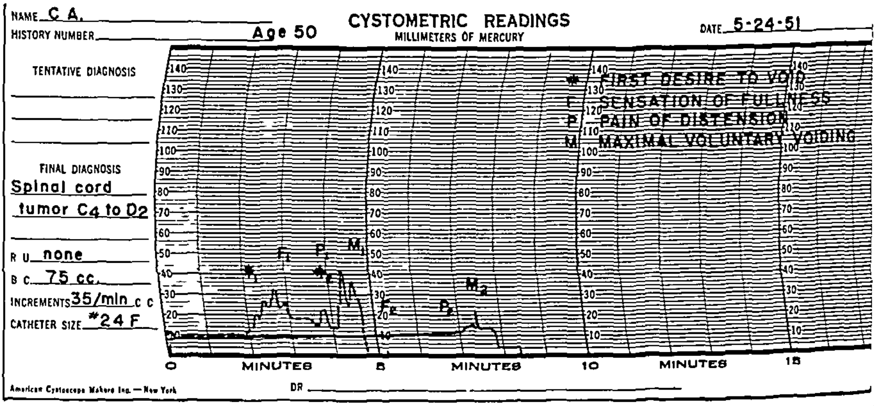
NAME C A.
HISTORY NUMBER Age 50
DATE 5-24-51
TENTATIVE DIAGNOSIS
FINAL DIAGNOSIS Spinal cord tumor C4 to D2
R U none
B C 75 cc.
INCREMENTS 35/min c c
CATHETER SIZE *24 F
DR

Fig. 10. Reflex neurogenic bladder (case 6) demonstrated in curve 1 (broken line). Inhibition of hypertonicity and increase in bladder capacity from 75 cc to 250 cc are noted after banthine, 25 mg. intravenously (solid line), but complete lack of sphincter control rendered drug therapy ineffectual.

DISCUSSION

Banthine bromide was found to have a profound depressant effect on the detrusor muscle in both normal and neurogenic bladders. The parasympathetic innervation of the detrusor can be partially blocked by this agent as evidenced by cystometrograms. Drug effects noted on a normal bladder (curve 2, figure 1) are those of delay in first desire to void, delay in the onset of painful distension

(P), and an increase in bladder capacity. In addition, maximal voiding pressure was diminished, and complete bladder emptying became impossible. Similar drug effects were demonstrable on uninhibited and reflex neurogenic bladders. Five cystometrograms, representative of these two groups of neurogenic bladder dysfunction, demonstrate banthine's depressant effect on the hyperactive detrusor state. Moreover, the inhibition resulting from a single 100 mg. oral dose was found to exceed seven hours, (fig. 3).

By utilizing the information gained from these cystometric studies, it was possible to control urinary frequency and incontinence in three selected cases. Case 1, an acquired uninhibited neurogenic bladder, was managed for a six day period by administering banthine, 50 mg., orally after each voiding. Excessive frequency was decreased, so that adequate bladder filling occurred and the approximate time of urination could be anticipated. Micturition was more easily initiated by suprapubic pressure at a time when bladder filling was approaching capacity and the effects of the inhibitory agent were diminishing. With discontinuance of banthine, frequency and incontinence returned and the nursing staff could no longer keep the patient dry. Case 2, a congenital uninhibited neurogenic bladder, posed a similar problem of daytime frequency and incontinence at night. Banthine, 100 mg., given orally every six hours, reduced the level of bladder irritability and stopped the frequent, urgent desire to void. The blocking of this patient's enuresis during the testing period was anticipated from the cystometrogram presented in figure 5. These findings are suggestive but inconclusive since the patient was lost for continued study by his untimely discharge from the hospital.

Reflex neurogenic bladders (cases 3, 4, 5) showed a favorable response to banthine as evidenced by cystometrographic measurements (figs. 7, 9, 10). Case 3, D. F., noted diminished urinary frequency coincident with increased bladder capacity while taking banthine. A particularly distressing, intermittent type of dribbling incontinence was much improved. A consideration of urinary continence from the standpoint of detrusor-sphincter balance, rather than from sphincter paralysis alone, will provide an explanation for the development of urinary continence in this patient. A hyperactive detrusor may simply overwhelm a weakened external sphincter. With control of the hyperactive expulsive force, an otherwise functionally inadequate sphincter may become competent during the period when the detrusor is depressed. Curve 1, figure 9, shows graphically the magnitude of these reflex detrusor contractions; pressures of 75 mm. of Hg are produced at the height of the contractions. The control of this involuntary hyperactivity by banthine as shown by curve 2, figure 9, favors bladder filling without abnormal stress tending to force open the sphincter mechanism.

Case 5 presented an additional problem. This 50 year old quadriplegic's sphincter mechanism offered no resistance to the outflow of urine and, consequently, inhibition of the detrusor did not control the constant urinary dribbling.

Certainly, not all neurogenic bladder problems will lend themselves readily to banthine therapy. The hypotonic decompensated detrusor will only be further compromised by banthine. Likewise, bladder neck obstruction constitutes a definite contraindication to this form of treatment. The presence of glaucoma or myasthenia gravis, at least from theoretical considerations, must be ruled out prior to the use of banthine.

Severe toxic symptoms from the drug have been noticeably lacking during the course of investigation, although dry mouth, dilatation of pupils, blurring of vision, tachycardia, and elevation of peripheral blood pressure have occurred with the intravenous injection of 25 to 50 mg. However, few complaints have been voiced by patients on oral doses of 50 mg. every six hours. The initial dose should be small (25 mg. every 6 hours) with subsequent increase until the desired effect is obtained.

Cystometrograms provide a ready method for the intelligent selection of cases and for evaluating the effects of treatment. Weyrauch et al.[5] have questioned the value of cystometrograms in the diagnosis of neurogenic bladder dysfunction. These criticisms are valid to a point, since in most instances a complete historical and physical survey, plus a cystoscopic examination, will provide ample evidence for diagnosis. Moreover, the cystometric curve is in itself only a recording of pressure changes in a viscus; it thus serves as a diagnostic adjunct. When coupled with subjective information secured from the patient during the period of bladder filling, this pressure curve becomes a graphic representation of bladder activity and bladder response to the influence of drugs. We have found the curves reproducible on repeated measurements.

After the judicious selection of cases, one can safely utilize the marked and prolonged inhibitory action of an anticholinergic agent such as banthine. A delay in the first desire to void and an increase in bladder capacity can be anticipated. Incontinence, due to a hyperactive detrusor overpowering a normal or slightly weakened external sphincter, may be corrected by the inhibitory action of banthine as restoration of detrusor-sphincter balance is obtained. The production of a residual urine has not occurred where the oral route was used unless a borderline bladder neck obstruction was present. One patient (D. F.) has been managed with banthine for a period of 5 months without ill effect.

The largest single factor which emerges from this study as an indication for anticholinergic therapy in the neurogenic state is hypertonicity of the detrusor muscle. It would appear from our studies thus far that the neurogenic bladder is much more profoundly affected by comparable dosages of banthine than is the normal bladder, and that amounts smaller than those anticipated from the effects on normal subjects are adequate to suppress involuntary contractions and increase bladder capacity in the hypertonic bladder. For example, banthine, 25 mg. intravenously, increased bladder capacity by amounts of 300 to 400 cc in neurogenic cases 1, 3, 4, and 5, as contrasted with increases ranging from 30 to 90 cc in normal bladders. Parenthetically, it may be noted that any increase in bladder capacity recorded on succeeding trials run in rapid succession is of more actual significance than is, at first glance, apparent since Rose has shown that such succeeding studies in hypertonic bladders, without other external influences, tend to show mild decreases in bladder capacity and a concomitant trend toward hypertonicity, due to irritation.

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[5] Weyrauch, H. M., Lucia, E. L. and J. Howard: Failure of the cystometrogram as a diagnostic test. J. Urol., **51:** 191, 1944.

It need hardly be emphasized that significant amounts of residual urine should be eliminated prior to the institution of anticholinergic therapy, since such therapy may be logically expected to increase the amount of residuum present.

SUMMARY

Banthine, an anticholinergic agent, exerts a profound depressant effect on the detrusor muscle in both normal and neurogenic bladders by producing a partial block of the parasympathetic innervation of the bladder.

Control of urinary frequency and incontinence was obtained with banthine therapy in the uninhibited and reflex neurogenic groups of bladder dysfunction.

The judicious selection of cases is necessary since there are definite limitations and contraindications to this method of therapy.

Cystometry proved to be a practical method for the selection of cases and for evaluating the effects of treatment.

No severe toxic symptoms, due to banthine, were encountered during the course of this investigation.

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BLADDER TUMOR IN CHILDREN; REPORT OF THREE CASES

R. DE SURRA CANARD AND J. E. RIVAROLA

Malignant bladder tumor is unusual in children and because of its rarity, we wish to report 3 cases of exceptional clinical interest. Beer and Hyman state (N. P. Rathbun):[1] "Tumors of the bladder in childhood are so rare that an extensive discussion of their symptomatology and treatment is scarcely necessary. . . ." Yet the observation of one case treated conservatively and with the regularly discouraging end result, together with the 100 per cent mortality in similar cases treated by others, has convinced us that such lesions must be tackled with a radical procedure. We have limited our present study to the myxoma type of tumor because the 3 cases here reported were of that pathologic variety. Rathbun's tabulation showed that the number of myxomas of the bladder in the young at that time (1937) was sixteen and myxosarcomas four. In table 1 are indicated the cases of vesical myxoma we found reported in the literature.

The origin of these tumors is likely to be embryogenic (Aschoff)[2] but the initiating cause is yet unknown. The site of the initial growth is usually in the trigone and the vicinity of the bladder neck. During its first stage of development, the tumor is pedunculated but with further growth becomes sessile. As Deming[3] observed, these tumors have a tendency to spread over the bladder surface and seldom penetrate the muscularis. In one case he operated upon by generous partial cystectomy, superficial extension of the tumor was discovered in what was considered healthy tissue. W. Usadel,[4] analyzing a series of myxomatous tumors in other sites, concluded that although they have a benign histologic aspect, they relapse locally even after extensive resection. Local and neighboring recurrence is the usual evolution of these tumors; metastasis occurs occasionally (Weiss and Dreyfus;[5] Lazarus and Rosenthal;[6] Descalopoulos[7]).

According to Usadel, the mortality in myxomas is due to cachexia induced by multiple recurrences, but sometimes results from the transformation of their original myxomatous nature into myxosarcoma. Bladder myxoma not only may undergo this evolution but, equally or even more important, regularly produces obstruction at the bladder neck or at the ureterovesical junction, or at both sites.

The symptoms of bladder myxoma are those of all bladder tumors in chil-

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The first case was presented at the Córdoba meeting of the Argentine Urological Society, and published in the Revista argentina de urología, July-December 1947. The other 2 cases were presented at the meeting of the Pan American Urological Society in Santiago, Chile, December 1949.

[1] Rathbun, N. P.: Surg., Gynec. & Obst., **64:** 914, 1937.

[2] Aschoff, L.· Anatomia Patologica Trattato per Medici e Studenti (Traduzione della seconda edizione tedesca), **2:** 499, 1914.

[3] Deming, C. L.: Surg., Gynec. & Obst., **39:** 432, 1924.

[4] Usadel, W.: Arch. f. klin. Chir., **189:** 708–712, 1937.

[5] Weiss, A. G. and Dreyfus: Rev. Franç. de Pédiat., **4:** 801–803, 1928.

[6] Lazarus, J. A. and Rosenthal, A. A.: J. Urol., **27:** 695–712, 1932.

[7] Descalopoulos: Arch. d. Mal d. Reins, **4:** 270–275, 1929.

TABLE 1

YEAR	AUTHOR	SEX	AGE	SYMPTOMS	LOCATION	DIAGNOSIS	OPERATION	METASTASIS	EVOLUTION
1891	Billroth	M	2 yrs.	Frequent hematuria	Base of bladder	Myxosarcoma	Extirpation cystectomy		Died
1891	Albarrán	F	1½ yrs.		Trigone	Myxosarcoma	None		Died
1892	Phocas	M	6½ yrs.	Hematuria	Trigone	Myxosarcoma	Perineal		?
1894	Southan	M	6 yrs.	Frequent incontinent dysuria	Entire bladder	Myxosarcoma	Suprapubic cystectomy		Died after 2 d
1895	Clado	M	2 yrs.	?	?	Myxosarcoma	?		?
		M	3 yrs.	?	?	Myxosarcoma	?		?
1896	Concetti	F	1 yr.	?	Trigone	Myxosarcoma	Cystostomy		?
1921	Deming	M	20 mos.	Dysuria frequency hematuria distressed	Base of bladder	Myxosarcoma	Cystostomy, partial cystectomy		Died after 11
1928	Weiss & Dreyfus	M	6 mos.	Obstructed cachexia	Posterior wall trigone	Myxosarcoma		Lung	Died after 1 m
1929	Montenegro	F	1 yr.	Dysuria hematuria incontinence	Base & neck of bladder	Myxosarcoma	Cystostomy Extirpation		Died after 2
1929	Descalopoulos	?	9 mos.	Obstruction abdom. tumor	Anterior surface	Myxoma	Cystostomy	Peritoneal	Died after 7
1931	Rizzi	F	2 yrs.	Dysuria frequency pain obstruction hematuria pyuria	?	Myxosarcoma	Cystostomy		Died after 7
1932	Lazarus & Rosenthal	M	2 yrs.	Hematuria frequency	Diffuse	Myxosarcoma	Endoscopy cystostomy X-Ray Radium	Kidney	Died after 11
1932	Weiss & Meyer	?	4½ mos.	Frequency dysuria	?	Myxosarcoma	?	?	Died after 1 uremia
1939	Ratliff & Valk	M	12 yrs.	Frequency distressed	Neck of bladder	Myxofibrosarcoma	?	Extension local	Died after op
1913	Meade	?	5 yrs.	Frequency hematuria	Trigone	Fibrosarcoma	Extirpation sub-mucous		?

dren: disturbances in bladder function with dysuria, frequency, acute then chronic retention, incontinence (overflow) and, less frequently, hematuria. Cachexia, anemia, gastro-intestinal disturbances with anorexia, "indigestion," biliousness, constipation, loss of weight or failure to gain reflect not only the toxemia of the growth but also that resulting from advancing renal damage caused by the increasing bilateral urinary obstruction. Urosepsis is the usual terminal condition.

Physical examination discloses a distended bladder (Montenegro)[8] or, by abdominal and rectal bimanual palpation after urination, a tumor mass corresponding to the bladder (Rizzi;[9] Weiss-Meyer;[10] and others). A variable *amount of residual urine is usually present.* The general condition of the child is largely dependent on the duration and rate of growth of the tumor. Sometimes in girls the first symptom is the protrusion of part or all of the tumor through the urethra as may occur with ureterocele (case 2).

Urographic examinations have not been mentioned in many of the reported cases; the condition of the upper urinary tract, especially the existence of lower ureteral obstructions by tumor growth, has largely passed unnoted.

Cystography is most useful; in our first case the density of contrast medium was irregular and according to the extension of the tumor. Usually the cystogram shows multiple round lacunar spaces (filling defects).

Cystoscopy discloses segmental vesical involvement; the appearance of the tumor has been compared by Montenegro to multiple cysts, by Lazarus and Rosenthal to edema, by Nitze[11] to a hydatidiform mole. The impression our first case gave us was that of looking inside a hydatid cyst full of daughter cysts.

The treatment of bladder myxoma has been generally fruitless. Verhoogen[12] advises partial cystectomy for a localized growth and for the "voluminous and extended tumor cystectomy *seems* to be the choice." Marion[13] suggests ". . . not to tackle the extended tumors" and considers them as nonoperable cancer. In the published cases, extirpation of the tumor, partial cystectomy, electrocoagulation and deep x-ray radiation therapy have been employed unsuccessfully with fatal relapses in every case except the one of Meade's[14] in which the ultimate outcome is unknown.

Concerning radical treatment (total cystectomy), Deming noted: "This procedure has not yet been tried although it has been suggested by Albarran and Darlington in 1905." Case 2 of the present report is unusual in that bilateral ureterosigmoidostomy and total cystectomy were used.

[8] Montenegro, A.: Rev. de Especialidades, 4: 1085–1087, 1929; also Semana Méd., 1: 241–242, 1930.

[9] Rizzi, R.: Arch. ital. di urol., 8: 306–336. 1931.

[10] Weiss, A. G. and Meyer, R.: Rev. Franç. de Pédiat., 8: 748–750, 1932.

[11] Marion, G., Heitz Boyer, M. and Germain, P.: Traité Pratique de Cystoscopie et de Cathétérisme Urétéral. I. Cystoscopie d'Exploration. Masson et Cie., Editeurs, p. 124, 1924.

[12] Verhoogen, J.: Neoplasmes de la Vessie. Encyclopédie Française d'Urologie, Edition Gaston Doin, 4: 524, 1921.

[13] Marion, G.: Tumeurs de la Vessie. Traité d'Urologie. Masson et Cie., Editeurs, vol. 1, p. 588, 1928.

[14] Meade, H.: Brit. J. Urol., 15: 10–11, 1943.

CASE REPORTS

Case 1. C. A., a 2-year-old boy, was brought to the Children's Hospital because of urinary incontinence (continuous dribbling) for 5 months. He complained of pain in the lower abdomen especially when moving his bowels. There was anorexia. Examination disclosed poor general condition and a distended bladder. The bladder urine was cloudy. After emptying the bladder, the abdominal tumor had less tension but its size remained unchanged.

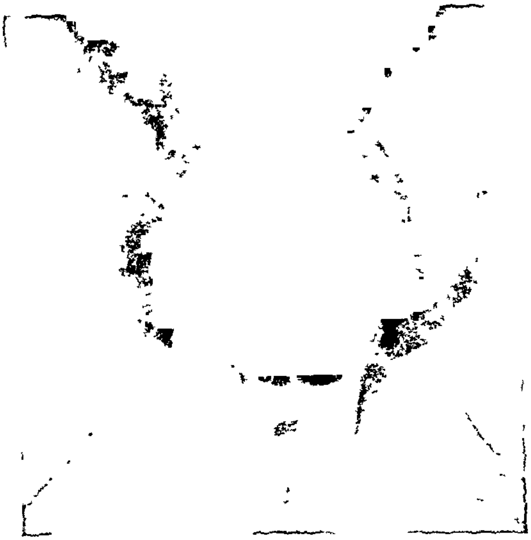

FIG. 1. Case 1. Cystography showing round lacunar spaces produced by tumor.

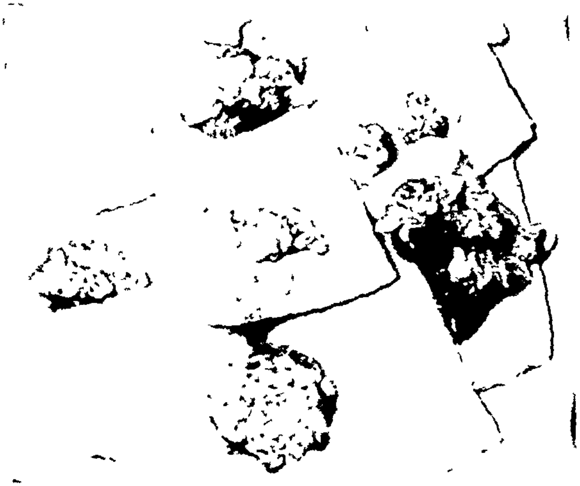

FIG. 2 Case 1 Grapelike tumor, free portions enucleated from bladder through cystostomy.

Cystoscopy revealed a bladder of low capacity (80 cc) and it was almost entirely occupied by multiple cysts: some of this cystic mass consisted of free grapelike vesicles. Excretory pyelography was negative after forty-five minutes. Cystography (fig. 1) disclosed a big bladder and irregularity in the density of the contrast medium (multiple ball like lacunar spaces) due to the tumor in the lower part.

Under ether narcosis, accompanied by blood transfusion, the bladder was opened and found to be almost totally occupied by a grapelike tumor, part of it free and easily enucleated with forceps (figs. 2 and 3). The remaining mass, with similar superficial characteristics, was adherent to the trigone and lateral walls. Complete excision of the tumor had been anticipated, but severe bleeding made this impossible. Pathologic report (fig. 4): Myxosarcoma.

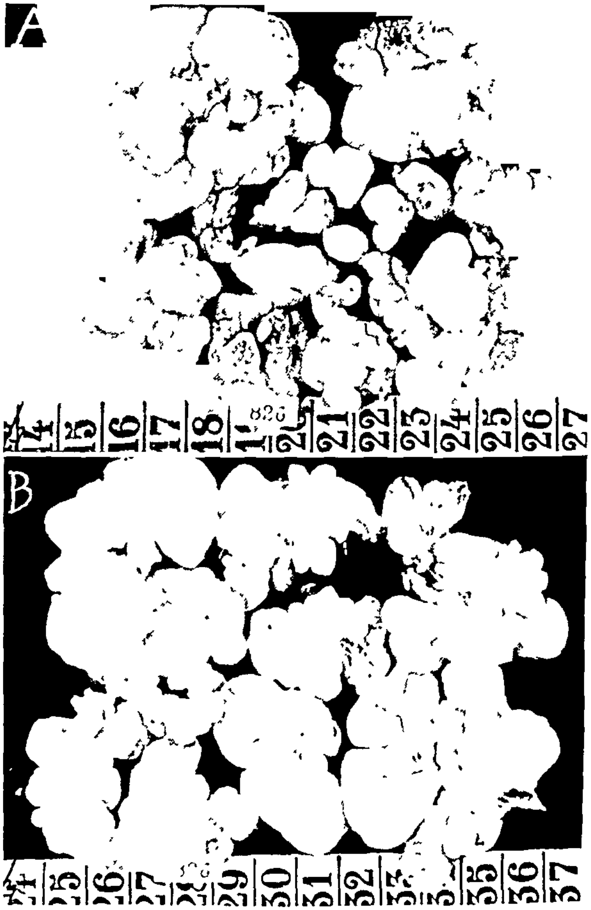

FIG. 3. Case 1. *A*, same tumor with metric scale. *B*, each piece cut in half shows solid tumor.

X-radiation therapy was given over a period of 72 days (5,350 r through four fields; 55 doses of 156 r each). Six months later the tumor prolapsed through the abdominal wound. The condition of the child was poor. A cutaneous ureterostomy of the greatly dilated right ureter was attempted; the urine in it was cloudy. The patient died on the operating table. No autopsy was permitted.

Case 2. D. J., a 2-year-old girl, was seen at the Children's Hospital because of a growth protruding through the urethra; the protrusion coincided with urinary retention and elevated temperature. Three months previously a similar growth had twice been excised. Tissue was excised from the growth for biopsy and, as the urethra had been widely dilated by the prolapsed tumor, it was easy to examine the bladder cavity by digital exploration. This disclosed a large tumor with many free grapelike cysts.

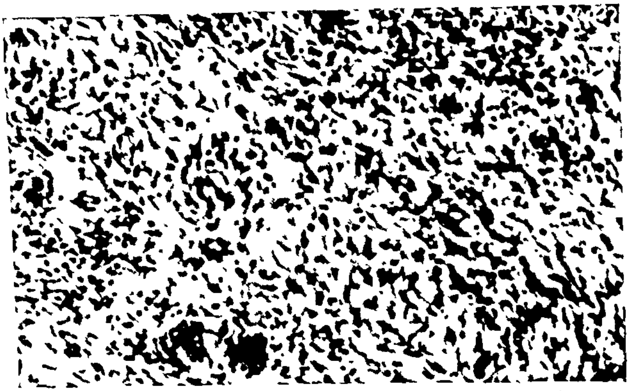

FIG. 4. Case 1. Histological detail. Myxomatous proliferating tissue with round-cell invasion.

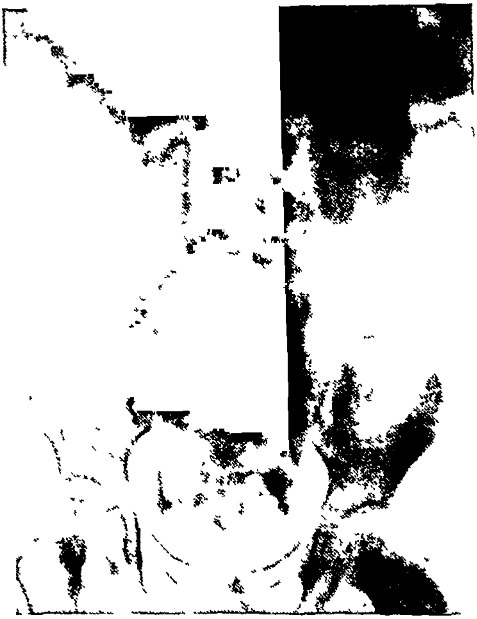

FIG. 5. Case 2. Excretory urogram. Good renal function. Distended bladder with lacunar spaces in lower half.

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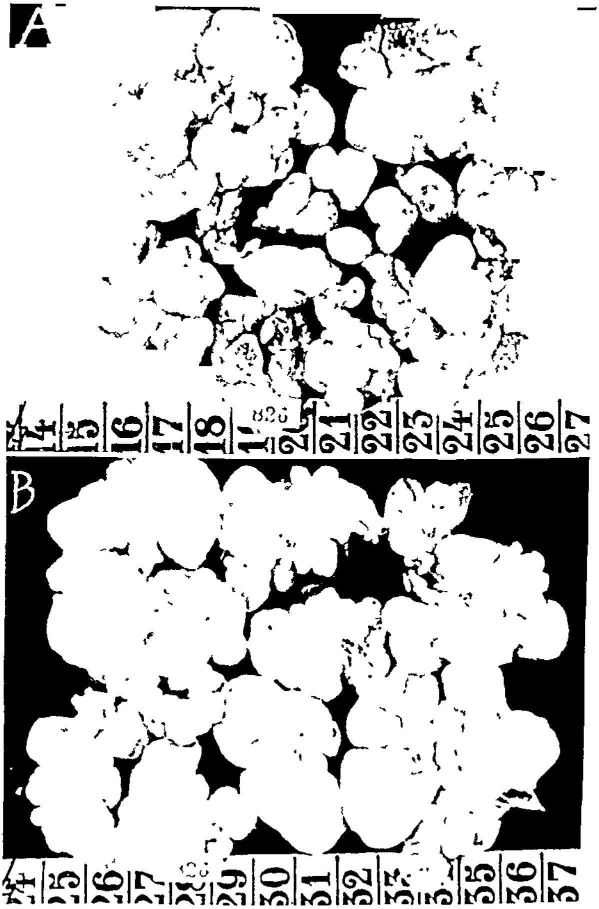

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(filling defects) in the lower segment and corresponding to the site of the tumor (fig. 5).

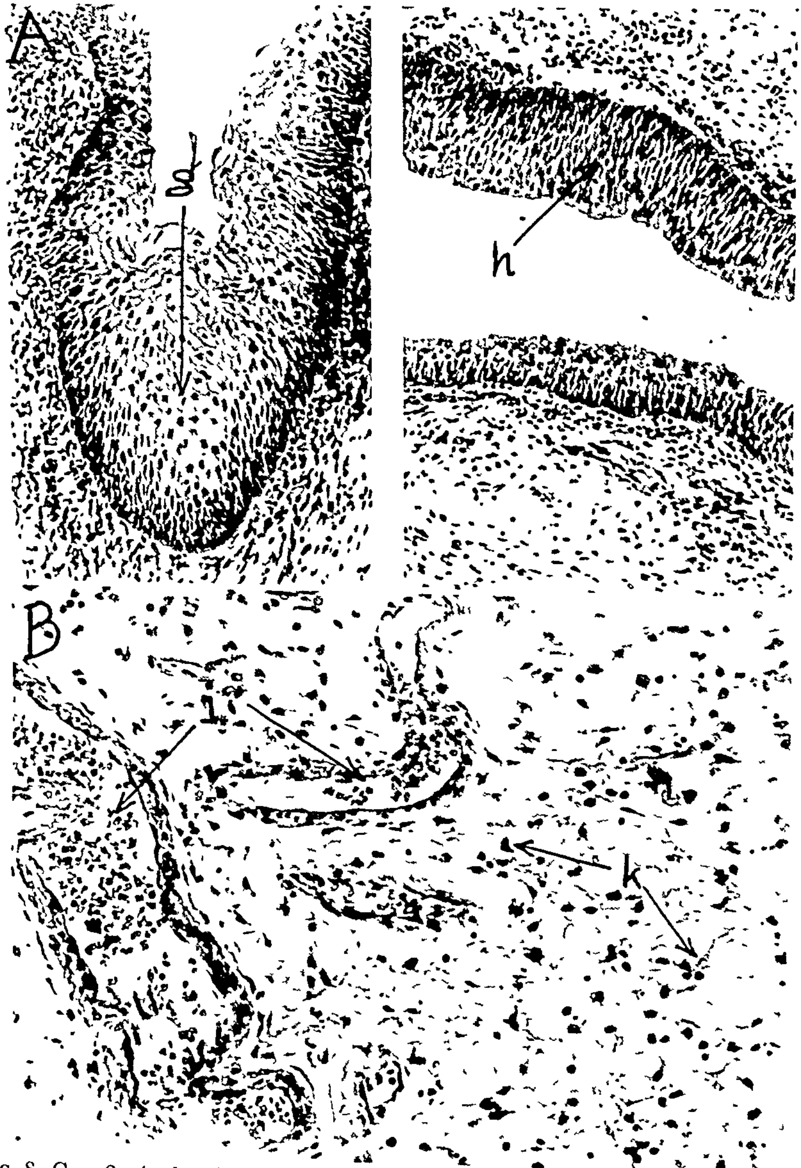

FIG 8 Case 2 *A*, detail of covering epithelial layer of polypoid tumor. *B*, detail of connective tissue, myxoid stellate cells

A total cystectomy was decided upon. At the first operation right ureterosigmoidostomy was performed and 3 weeks later, left ureterosigmoidostomy. Two weeks after the secondary ureteral transplant, total ureterocystectomy was carried out. The surgical specimen is shown in figure 6.

The tissue removed consisted mainly of connective tissue covered by normal vesical epithelium and in certain areas evidence of malignancy.

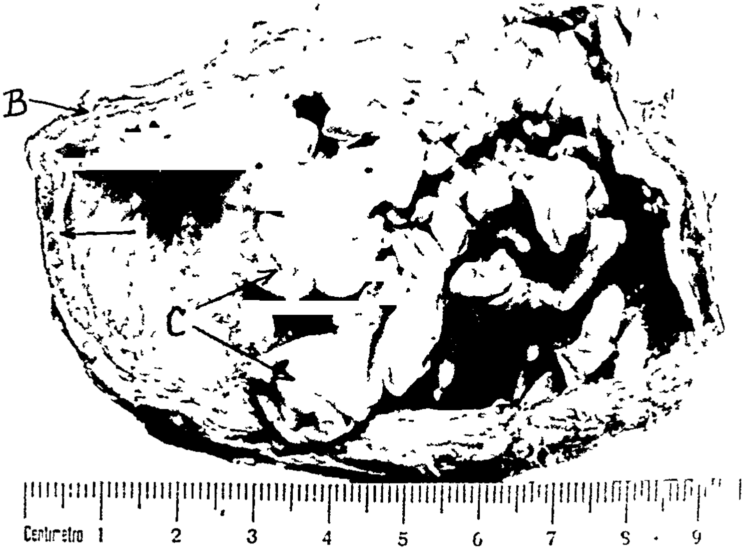

FIG 6 Case 2 Whole bladder with tumor obtained through surgery

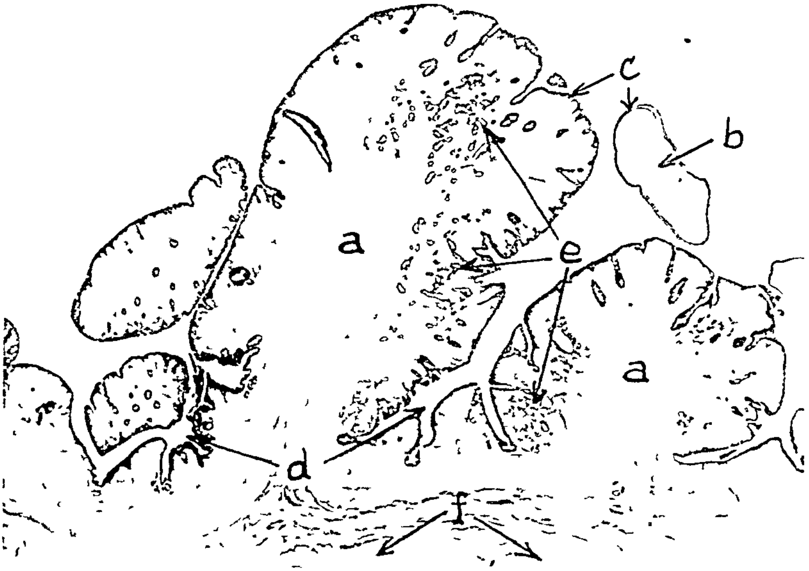

FIG 7 Case 2 Detail of polypoid tumor and bladder wall

Cystoscopy showed a normal bladder neck and in the bladder a cystlike tumor similar to that described in case 1.

Excretory urography was normal in regard to the kidneys and ureteral morphology and function. The excretory cystogram disclosed many lacunar spaces

Case 3. A 6-year-old boy was brought to the Children's Hospital by Dr. José Pelliza with the history that the mother had noted the patient's daily output of urine was markedly reduced and his condition progressively poorer. There was great difficulty in micturition.

On physical examination rales were heard over the entire lung field. The cardiac action was normal. A huge tumor filled the distended lower abdomen. There was edema of the external genitalia and the superficial cutaneous venous circulation was engorged. By rectal examination the tumor was found to bulge into the pouch of Douglas. It was impossible to pass a sound to the bladder because of obliteration of the posterior urethra by tumor growth and compression.

Because of progressive tumor growth and rapid decline of the boy, an exploratory laparotomy was performed. The superficial layers overlying the bladder were infiltrated with tumor and all of the greatly distended bladder was transformed into fragile friable cephaloid tumor tissue. On opening the viscus, a small amount of urine escaped. The whole bladder was found occupied by tumor tissue, part of it free in the cavity, but most of it adherent to the walls (fig. 10). Considering further surgery useless, a cystostomy drainage tube was left in the bladder and the wounds were closed. The boy died 4 days postoperative.

DISCUSSION

This experience limited to 3 cases of bladder myxoma in children justifies no conclusions, but we gained suggestive evidence in 1 case of the potential benefit of total cystectomy. In our first case we used conservative surgical treatment (cystotomy drainage) as described by others; the result was several months of suffering for the child, ending in customary failure. In our second case in which total cystectomy was performed, the patient did well for 12 months and, until intestinal occlusion occurred, her general condition was excellent. The far-advanced growth of the tumor in the third case permitted only the establishment of the diagnosis, and the institution of free bladder drainage.

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Microscopic examination of the tumor showed a polypoid growth with a thickened epithelial layer with connective tissue and myxoid stellar cells beneath (figs. 7 and 8).

Postoperatively the child did well and her general condition was excellent. Excretory urography 2 months after the operation showed dilatation of the upper urinary tract with satisfactory function (fig. 9). One year postoperative the mother reported that the child, although her condition was satisfactory, had complained on several occasions of abdominal distention and there had been vomiting and fever, followed by violent bowel discharges. Examination revealed a distended abdomen with pronounced dilatation of the superficial venous circulation. Upon rectal examination a large tumor was felt in the pelvis.

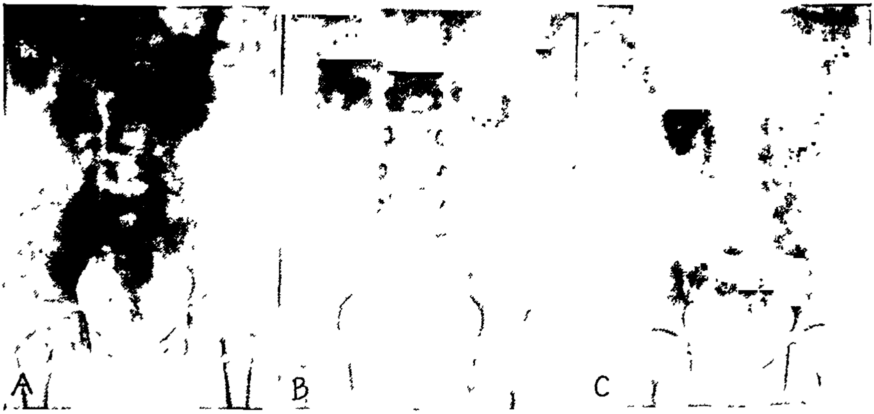

FIG. 9. Case 2. *A*, excretory urogram 2 months after total cystectomy. *B*, excretory urogram 8 months after operation. Slight urethral dilation and displacement of left ureter outwards. *C*, excretory urogram 12 months after operation. Major displacement of both lower ureters.

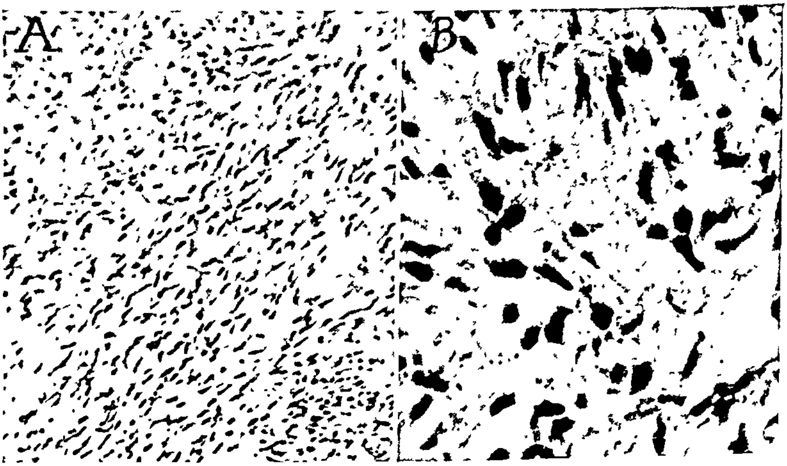

FIG. 10. Case 3. *A*, stellar cells among fibular tissue. *B*, high power.

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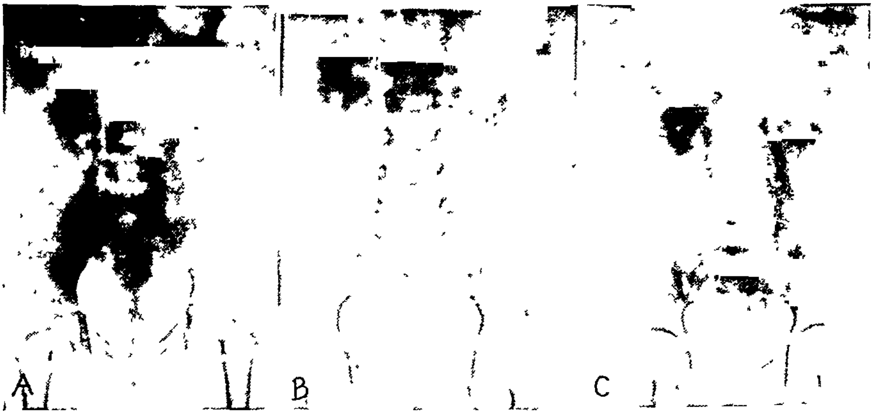

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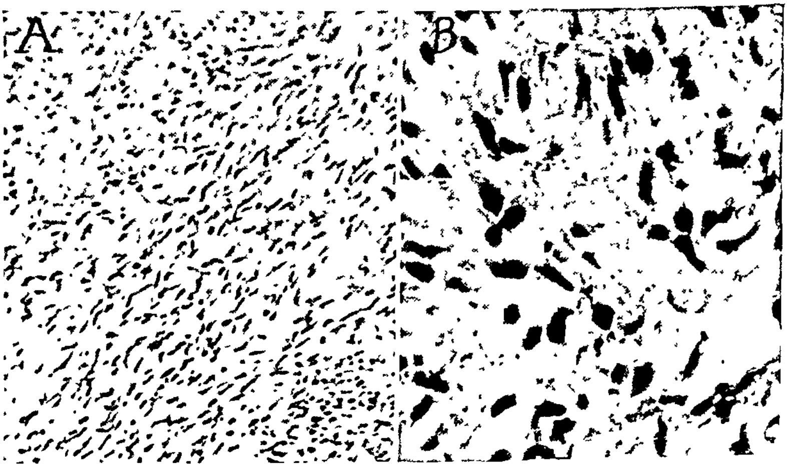

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INGUINAL HERNIA AND BLADDER DIVERTICULUM

PETER L. SCARDINO AND THOMAS E. UPSON

The urinary bladder is not infrequently encountered in herniotomy. However the occurrence of a bladder diverticulum in association with an inguinal hernia is an uncommon surgical experience and one which requires the combined efforts of the surgeon and the urologist. A review of urologic literature reveals a single recent American report of "scrotal cystocele" in which the author reported 2 cases of his own and found 30 others in the foreign literature.[1]

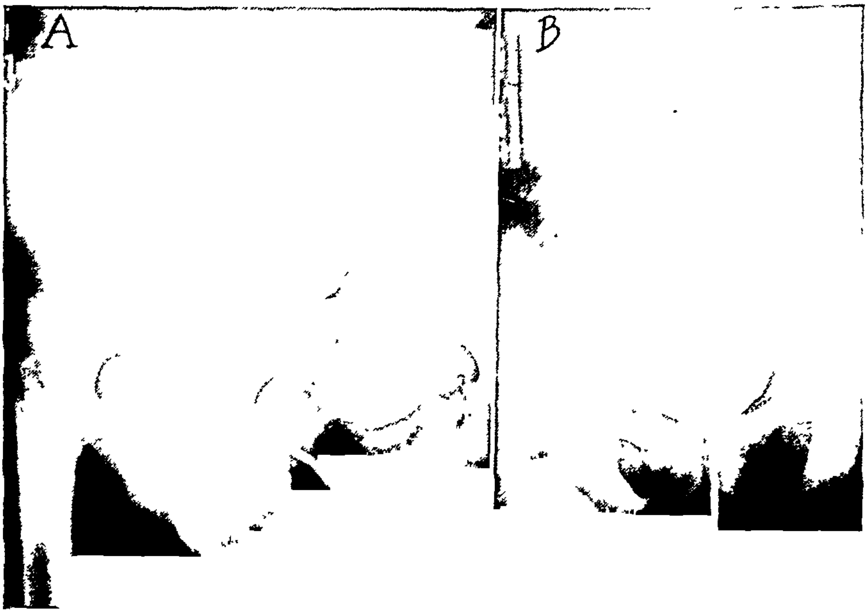

FIG. 1

While a careful history and physical examination will, in most instances, reveal the presence of a bladder diverticulum, exact diagnosis can be made by cystographic studies. Once an accurate diagnosis has been established, the combined surgical-urological team can plan a surgical approach compatible with simultaneous repair of the hernia and bladder diverticulum. Failure to establish the diagnosis prior to surgery is an invitation to surgical difficulties.

CASE REPORT

A 59 year old white married man was admitted to the hospital complaining of a swelling in the right side of the scrotum of 5 years' duration. He had noted that this mass gradually increased in size and concurrently became associated in its growth with urinary symptoms. While there had been no frequency of urination, urgency, hesitancy or dribbling which might have suggested prostatism, he

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[1] Levine, B.: Scrotal cystocele. J.A M.A., 147: 1439, 1951.

had noted intermittency. He had found it necessary after each voiding to complete the act by applying pressure to the scrotal mass which then became reducible. Otherwise he was unable to reduce the scrotal mass without inducing a desire to void. The past history revealed an unsuccessful repair of a right inguinal hernia 8 years previously. Examination was noncontributory except for the presence of the partially reducible inguinal hernia on the right associated with a right scrotal mass which was reducible following micturition. The diagnosis of inguinal hernia associated with bladder diverticulum was readily established by a cystogram (fig. 1, *A*). Cystoscopic examination failed to reveal evidence of vesical neck or prostatic obstruction.

On February 8, 1952, three days following hospital admission, the patient underwent repair of the right inguinal hernia and excision of the diverticulum. Under general anesthesia a right inguinal incision was made in the usual fashion exposing the hernial sac which was in juxtaposition to an enormous bladder diverticulum. After excision of the sac in the usual manner, the poorly defined fascial structures were repaired with interrupted cotton sutures. The inguinal incision was carried distally and medially. The right rectus muscle was divided. This permitted excellent exposure of the dome of the bladder and the neck of the diverticulum. A cystostomy was performed after which the mouth of the diverticulum was readily identified in the right lateral bladder wall and circumcised from within the bladder carrying the incision through the musoca, muscularis and aventitia after which the diverticulum was excised en masse. A continuous zero plain catgut suture approximated the bladder mucosa. The bladder musculature and adventitia were approximated with a continuous chromic 1 catgut suture reinforced with a second layer of interrupted chromic 1 catgut sutures. Examination of the right ureter revealed it to be intact and uninjured. The cystostomy was closed with chromic 1 catgut sutures around a 28F mushroom catheter. The divided rectus fascia was approximated with interrupted chromic 1 catgut sutures. Drains were placed in the space of Retzius and adjacent to the right lateral bladder wall. Both drains were brought out the lower angle of the wound. The skin edges were approximated with interrupted cotton sutures. A 22F, 30 cc bag catheter was inserted into the bladder through the urethra and inflated. Both catheters drained well. The suprapubic catheter was removed 7 days postoperatively. The urethral catheter was removed on the fourteenth postoperative day. One month postoperatively the herniotomy and suprapubic wounds were healed. Urinalysis was negative. The patient's only urinary symptom was nocturia 1 time. A postoperative cystogram revealed a normal bladder (fig. 1, *B*).

COMMENT

Cystographic studies are indicated prior to inguinal herniorrhaphy in those patients whose history and physical examination suggest a urinary condition.

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THE NESBIT SIGN

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To expedite transurethral prostatectomy, an accurate constant picture of the whole operating field is absolutely necessary. Recognition of bladder wall, trigone, bladder outlet, pathologic anatomy of the prostatic urethra in all its various possibilities, the verumontanum, the character of the cut surface of the benign, fibrous and malignant prostatic tissue and the surgical capsule of the prostate comes automatically to the experienced resectionist. To these commonly recognized landmarks and characteristics I wish to add another which I think may rightly be called "the Nesbit sign." For several years Reed M. Nesbit has observed and shown his residents that the mucosa of the membranous urethra, particularly the floor, scuffs up or builds up ahead of the short beaked sheath of the resectoscope while being introduced whereas in the prostatic urethra this does not occur.

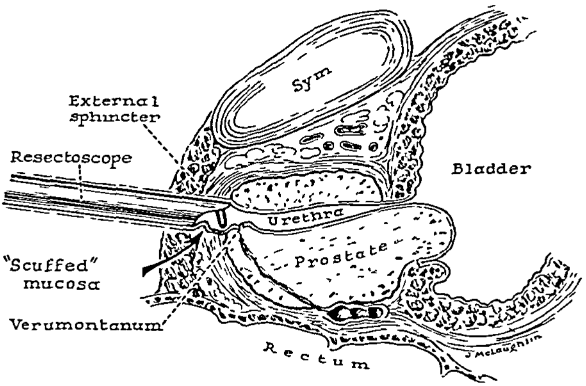

FIG. 1. Sagittal drawing of prostatic and membraneus urethra illustrating "scuffing" of mucosa of membranous urethra.

This mucosal characteristic is based on normal histology. As is shown in figures 1 and 2, at the junction of the membranous and prostatic urethra the mucosa of the membranous urethra is attached loosely, while that of the prostatic urethra follows the ducts becoming a part of the gland, and is firmly attached.

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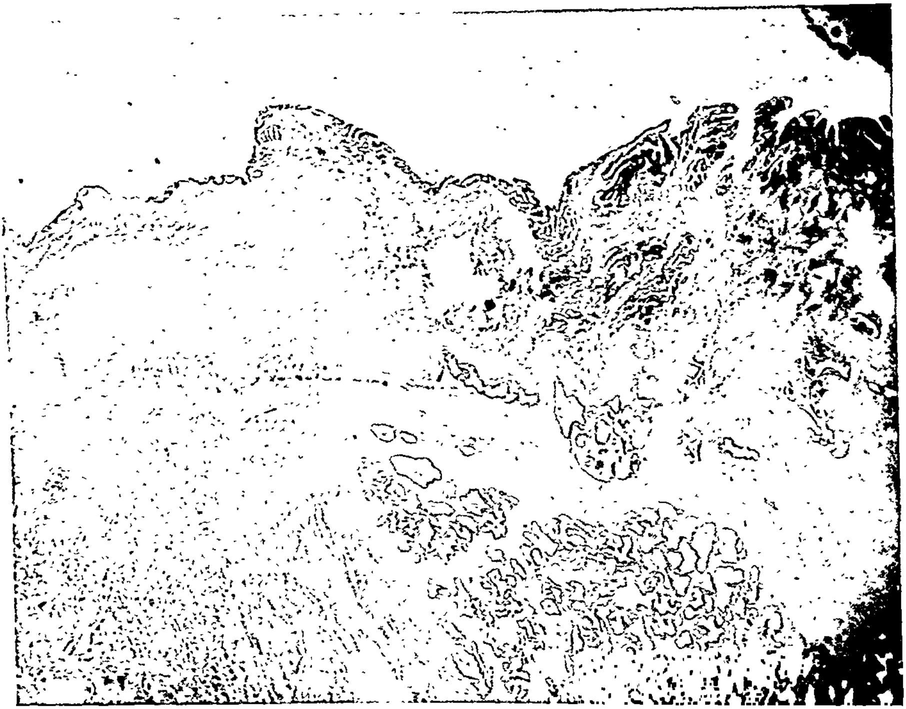

FIG. 2. Photomicrograph taken at juncture of membranous and prostatic urethra demonstrating immovable fixation of prostatic mucosa as compared to loose fixation of mucosa of membranous urethra.

This variation thus accounts for the scuffing in one part of the urethra and not in the other.

The recognition, then, by the resectionist of this normal anatomical variance gives him another landmark whereby he may be guided in his operation.

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MALIGNANT MELANOMA WHICH HAD ITS FIRST CLINICAL MANIFESTATIONS IN THE PROSTATE GLAND

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Melanoma of the prostate, as far as can be determined, has never been reported in the literature. The following case appears to be of sufficient interest to warrant recording.

CASE REPORT

A. McG., a man aged 38, was admitted to the Urological Service at the Kingston General Hospital, June 1, 1946. He gave a history of painful, frequent urination since September 1945. Shortly after the frequency began, he began to notice urgency which increased to the point of incontinence. He first consulted a urologist in November 1945, who attempted to do a cystoscopic examination but was unsuccessful and nothing further was done until March 1946, when the vesical discomfort became almost intolerable. He consulted another urologist who made a diagnosis of cancer of the bladder and inserted a suprapubic tube. A diagnosis of melanotic sarcoma was made on the biopsy taken at this time.

The patient's previous history was not significant. He had always been a sensitive, nervous type and suffered from attacks of petit mal. These had been controlled by barbiturates. His health had been as good as usual, although he had tired readily for some time prior to the onset of his vesical symptoms.

General physical examination showed a thin, healthy looking individual presenting no significant abnormal findings. Blood count and blood urea were normal. Cystoscopic observation revealed a large, sloughing tumor of the base of the bladder and vesical neck. A moderate degree of dilatation was present in the upper urinary tract.

Insertion of the suprapubic tube, rather than lessening the patient's troubles, as might have been expected, had only multiplied them. It was constantly blocking and leaking and he was suffering a great deal of distress both physical and mental. A bilateral cutaneous ureterostomy was decided upon and carried out June 4, 1946. At the same time the pelvis was examined to determine the feasibility of cystectomy. There was no evidence of infiltration of the peritoneum over the bladder but some enlarged glands were found at the bifurcation of his left iliac artery. These were removed and microscopic examination showed them to be inflammatory with no evidence of growth. Three weeks later a cystoprostatectomy was done. At operation it was found that the tumor had involved the capsule of the prostate. Histological studies showed it to be a malignant melanoma.

The patient made a good recovery, his general health improved and in 2 months he was back at work. He remained well until January 1947, when a small bluish spot appeared on the skin close to his right ureterostomy. This was excised and proved to be malignant melanoma also. Thorough physical examination failed to disclose any evidence of a primary growth. The patient remained

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well for another year when a second lump appeared in the upper right rectus muscle. This, too, was excised and was of the same nature as the other tumors. Again no evidence of a primary growth could be found. From this time on, numerous growths began to appear in various parts of his skin. The patient complained of many aches and pains, and his health gradually deteriorated. He slowly became more and more cachectic and died March 15, 1949.

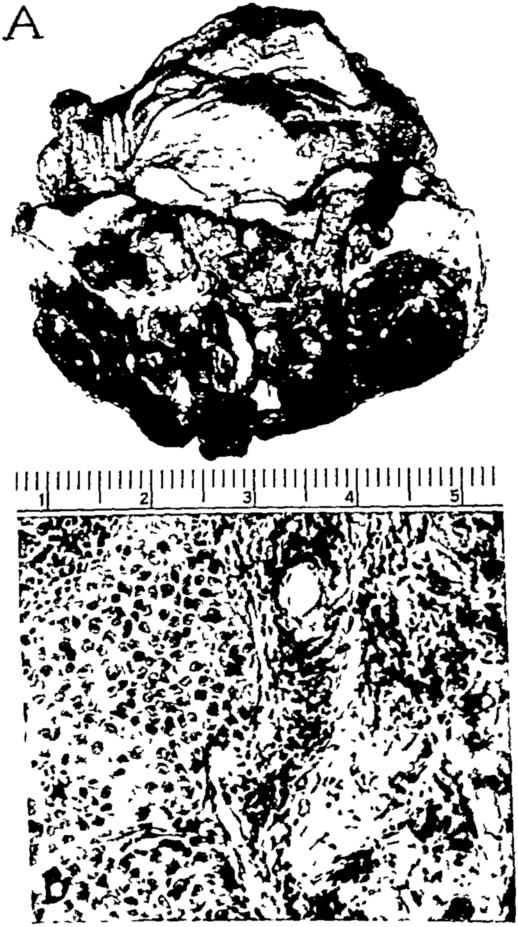

FIG. 1

The cystectomy specimen was examined in our laboratory on July 17, 1946, S-1889–46 (fig. 1, *A*). Grossly the specimen consisted of a urinary bladder, prostate, and seminal vesicles which had been previously fixed in formalin and opened anteriorly along the midline. The bladder was contracted and its capacity reduced to about 50 cc. The wall was thick and measured 1.5 cm. in thickness. The mucosa was intact and thrown up into folds. The floor of the bladder was elevated in a nodular fashion by the tumor mass in the prostate, which had infiltrated the muscular and subepithelial layers of the bladder wall, but did not break through the mucosal epithelium. Normal prostatic tissue was not grossly recognizable because the entire gland had been replaced by tumor. The prostatic urethra had been laid open. On its right side there was a tumor mass 4 by 3.5 by 1.5 cm., and on its left side there was a mass 4 by 4 by 3.5 cm. There were several hard, pale nodules, but the greater portion of the tumor was dark and friable. Posteriorly, the growth infiltrated through the prostatic capsule and upwards to surround the left seminal vesicle. The right seminal vesicle was not involved. The tumor was beginning to encroach on the ureters but a probe could readily be passed through the ureteral stumps into the bladder. The membranous urethra was replaced by tumor.

Microscopic sections showed no prostatic acini, as it had been entirely replaced by tumor. The tumor had also invaded the bladder musculature and subepithelial tissue and had invaded into and around the left seminal vesicle and vas deferens.

The tumor was variegated in appearance (fig. 1, *B*). In areas the cells were arranged in masses showing alveolar groupings separated by a fine stroma. In other areas they were arranged in cords. But, whatever their configuration, they were always invasive. The cells varied markedly in size and shape, but the predominant cell was a large, polyhedral cell with a large vesicular nucleus and a prominent nucleolus. The nuclei varied in size, shape, and staining intensity. The cytoplasm was scanty and acidophilic. Some areas showed large amounts of melanin pigment in the cells whereas other areas were nonpigmented and appeared carcinomatous. The tumor showed areas of necrosis and hemorrhage, where collections of hemosiderin were found. Silver stains showed a moderate number of argyrophillic fibrils interwoven around tumor cells. Diagnosis: Malignant melanoma of prostate.

The skin biopsies K.G.H. S-32-47 and K.G.H. S-66-48 taken on January 7, 1947, and January 12, 1948, respectively, showed a similar microscopic picture.

On March 16, 1949, a post-mortem examination was performed at the Ottawa Civic Hospital. The brain was not examined because of the objections of the patient's relatives; otherwise, the examination was complete. Scattered over the skin there were several small bluish-black, circumscribed areas measuring approximately 0.5 to 1.5 cm. in diameter. One large area 5 cm. in diameter was located on the posterior chest wall. The lungs were peppered with firm, black masses measuring 2 cm. in diameter. The mediastinum as well as the thoracic wall contained tumor tissue. Several secondary deposits were found in the heart muscle, as well as one large nodule in the endocardial surface of the left ventricle. The latter finding probably accounted for the widespread dissemination of tumor tissue. The liver weighed 2400 gm. and was composed almost entirely of tumor tissue. The adrenals together weighed 120 gm. and contained tumor tissue. The kidneys were invaded by neoplastic tissue also. The site of the bladder, prostate and posterior urethra was replaced by a massive, soft, necrotic, greyish yellow tumor. Here it remained fairly well localized, though multiple distant metastases as aforementioned were encountered. The para-aortic lymph nodes were replaced by tumor. Examination of the eyes failed to show any evidence of melanoma. The microscopic picture was similar to that already described for the surgical specimens.

DISCUSSION

The pathogenesis of malignant melanoma is still debated. Recently Allen, in a review of the melanomas, presented reasonably convincing evidence of the epidermal origin of such tumors, and stated that melanomas always arose from pre-existing "junctional naevi." It is possible that through a process of metaplasia of epithelium in either posterior urethra or prostate, a junctional change could occur, and thus give rise to the tumor under discussion.

No evidence of metaplasia could be found in the urethra, bladder of prostate but then the tumor was so extensive that no normal prostatic tissue was seen, and the lining epithelium of posterior urethra had been destroyed.

Masson considers that melanomas are neurogenic in origin, and arise from sensory end organs. If one considers the embryological development of the genito-urinary tract, Masson's theory of origin can still be applied to the case under discussion.

In the development of the genito-urinary tract, that part of the gut which lies caudal to the allantois is termed the cloaca. This is partitioned into ventral and dorsal portions by a mesodermal septum. The dorsal portion becomes the rectum, and the ventral portion forms a dilated upper part, the bladder, and a narrow lower part, the urogenital sinus. Prior to this division, the ventral wall, the cloacal membrane, consists of closely applied entoderm and ectoderm with no intervening mesoderm. This area in the adult is represented by the area between the symphysis pubis and the coccyx. When the septum which subdivides the cloaca reaches the cloacal membrane it divides it into urogenital and anal membranes. About the eighth week of intra-uterine life the urogenital membrane breaks down and the bladder acquires an opening in the perineum. The opening is on the caudal surface of the rapidly expanding ectodermal phallus. The two grow at the same pace so that the entodermal urethra is first a trough on the ventral aspect of the ectodermal phallus, before it closes over from posterior to anterior. The prostatic glands are buds at the entodermal urethra on which mesenchyme condenses to form muscle and fibrous tissue.

If we subscribe to either the epidermogenic or sensory end organ origin, there is ample opportunity in the development of the genito-urinary organs for ectodermal cell rests to occur and subsequently give rise to a melanoma.

Melicow tells us of a series of 300 melanomas in which careful search had failed to demonstrate the primary origin of the tumor in 80 cases. Orth and Neuberg found melanomas in the adrenal and nowhere else. Davidson found one large tumor in the adrenal and many small ones in the brain and colon. Weitling and Handi reported a supposed primary melanoma in the gallbladder, that being the only tumor which they found at post-mortem examination. Ewing reported a melanoma of the spleen with no other demonstrable tumor.

Our patient, at the time of operation in 1946, presented a malignant melanoma of his prostate gland. A careful search revealed no other melanotic lesion. He denied ever having had a skin lesion excised or cauterized. At post-mortem examination, 3 years later, the bladder and prostatic bed showed tumor and a disseminated melanosis was present. The post-mortem study was complete with the exception of the brain. Careful study of the tumor still gave the impression that the primary site was in the prostate. Had the primary site been in the brain, neurological symptoms should have been apparent. The eyes were free of tumor and we were satisfied of the absence of a skin lesion, past or present. The prostate as a site for secondary tumor except in cases of direct extension is most rare, and so lends weight to our contention that the melanoma arose in this area.

Believing this to be a case of primary carcinoma of the bladder involving the prostate, a radical cysto-prostato-vesiculectomy was carried out. The patient had 2 comfortable years of life following the procedure and lived nearly 3 years before dying from melanosis. Little doubt exists that the patient would have lived no more than a few months without surgery, as the tumor was already causing ureteral obstruction. This case again points out the value of radical surgery even when all that can be expected is palliation.

The primary site of this tumor is open to question. Campbell and Fein have reported a case of primary melanoma of penile urethra, and Melicow, in a personal communication, has seen one case on the glans penis in a 44 year old patient but no reported case of primary melanoma of prostate has been found. It is our impression that the case herein reviewed might be an example of primary melanoma of the prostate, but bearing in mind how frequently the primary site cannot be determined in these cases we admit that proof is lacking. We have been unable to find any reference to primary melanomas of the prostate or bladder in any of the standard texts.

SUMMARY

A case of malignant melanoma of the prostate is presented. As far as we can determine from a survey of the literature, this is the only reported case.

A brief discussion of the pathogenesis of melanoma and of genital embryology is presented in an effort to justify a diagnosis of primary malignant melanoma of the prostate.

We would like to express our thanks to Dr. John Hamilton, Professor of Pathology at Queen's University, and to Dr. M. Klotz, head of the Pathology Department of the Ottawa Civic Hospital, for their help in preparing this paper.

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DIVERTICULUM OF THE MALE URETHRA

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Diverticulum of the male urethra is rare. Undoubtedly many more instances have occurred than have been reported, but up to January 1951, Pate and Bunts were able to find only 197 cases in the extant literature. They added 28 cases of their own bringing the total to 225. All of their cases were of traumatic origin and followed peri-urethral abscess in paraplegic patients (i.e. trauma from infection). Since the *Cumulative Quarterly Index Medicus* has not been published in the past few years, and because of the interruption in the exchange of scientific data caused by world conditions, any review at this time must needs be incomplete. The author has, however, collected 8 cases since Pate and Bunts' excellent review, and these with the two cases to be reported in this paper, bring the grand total to 235 cases of diverticula of the male urethra.

Diverticula of the female urethra are not uncommon. This is not surprising when one considers the tremendous trauma brought to bear on the inferior surface of the female urethra which is at best anatomically poorly supported.

The male urethra, on the other hand, is anatomically very well protected against herniation. The dense and compact protection afforded the posterior urethra by the enveloping prostate are more than adequate. The membranous urethra is surrounded by the tough components of the pelvic fascia and the *sphincter membranaceae urethrae* with its investing fascia. The bulbous and pendulous urethra are both surrounded by several layers of dense fascia, and, in addition, are imbedded in the corpus spongiosum with its tough, fibrous, trabeculated vascular tissue.

An accolade to the toughness of the fascial supports of the cavernous urethra is evident in the innumerable inept soundings performed daily with perforation and false passage formation. These false passages are a common observation in the routine cystoscopies of any large clinic, and yet from these violations of the fascial confines of the urethra, only rarely do diverticula develop which are of any clinical significance.

ETIOLOGY

The rarity of the lesion precludes the acceptance of trauma and back pressure per se as the only reasons for this disease. Back pressure from simple urethral obstruction, due either to stricture or clamps or stones, does not give a satisfactory answer because this type of obstruction is very commonly seen with disastrous trabeculation of the bladder and hydro-ureter, and yet no diverticulum formation is noted in the urethra.

The number of Cunningham incontinence clamps used in the last two decades ought to have increased enormously the number of urethral diverticula encountered, yet statistically, and by personal observation this is not true. In view of this, reasons must be postulated or established why in one patient a diverticula develops shortly after using a clamp, and yet another will use a clamp for a number of years without any observable ill effects on the urethra.

That congenital diverticula without any existing obstruction distal to them do occur is a fact from observing case 1 in this paper and the reports of several others. Embryologically, Johnson demonstrated definite cystic epithelial lined structures just beneath the floor of the distal urethra, some of which communicated with the ureteral lumen to form small diverticular-like structures. The formation of the floor of the urethra by midline fusion is fraught with possibilities of an area of non or incomplete fusion which could be covered over by the mesenchyme and ectoderm and become clinically evident in later years when a distal urethral obstruction developed. Taking this a step further, one can easily visualize an area which has a deficiency of either endoderm or mesenchyme or both being covered by the ectoderm and remaining as an undetected weak point vulnerable to outpouching under stress. In effect, congenital diverticula and these weakened areas are nothing more than covered over hypospadias.

Fagerstrom postulates the theory that injury to the nerves to the urethra as they course past the prostate on their way to the urethra deprives the urethral wall of its tone and leaves it vulnerable to the development of herniations. This seems to be borne out more clearly in the series that Pate and Bunts reported. They found a high incidence of diverticula following peri-urethral abscess in the paraplegic patients (26 to 54 patients with peri-urethral abscess developed diverticula). This certainly is not in keeping with the general observations of the follow-up of peri-urethral abscess, and can be explained only on the interference in the tonus of smooth muscle, and tissue in general in these paraplegic patients.

That considerable nerve injury occurs in a radical perineal prostato-seminal vesiculectomy cannot be gainsaid. However, since large numbers of radical perineal procedures of this type are performed, and actually, large numbers of them do use clamps if not indefinitely, certainly in the early stages of temporary incontinence, and since diverticula are rarely seen under these circumstances, nerve injury alone cannot be the sole factor. In Pate and Bunts' group there was obvious trauma coupled with nerve injury; in others, it is most likely nerve injury coupled with embryological deficiency.

A third factor to be considered is the use of estrogens (case 2). It has been my observation that there is a decided prolongation of incontinence in patients who have had total perineal prostato-seminal vesiculectomy and who have been given postoperative estrogen therapy for cancer of the prostate. This is probably caused by the relaxation of smooth muscle and fibrous tissue induced by this hormone. Case 2 shows this action very well, for after diverticulectomy, the patient was completely continent except for occasional drops occurring after heavy lifting or severe straining. He had not had stilbesterol at this time for several weeks. The drug was renewed because of apprehension that recurrence of cancer might occur, and within 48 hours, he became completely incontinent. Reduction in dosage ameliorated the condition and a trial withdrawal resulted in return of control. This return of sphincter tone has been observed several times on other patients and is too consistent to be regarded as coincidental.

Therefore, this tissue relaxing action could start a congenital weakness herniating and result in a full fledged diverticulum under conditions of minimal stress.

Watts' original classification, which is very complete and which has served as a model for classifying diverticula of the male urethra, follows:

A. Congenital diverticula
B. Acquired diverticula due to:
  1. From dilatation of the urethra due to:
    a. urethral calculus
    b. urethral stricture
  2. Perforation of the urethra from:
    a. injuries to the urethra
    b. rupture of abscesses into the urethra
    c. rupture of cysts into the urethra

From the conclusions drawn from the other reported cases and those observed here, this list can be narrowed to two categories:

A. Congenital diverticula
  1. Those present without obstruction or influence of hormones or nerve injury. Most of these are noted as incidental findings or appear early in life.
  2. Those appearing clinically after the introduction of the agents mentioned in the previous sentence.
B. Traumatic diverticula
  1. Mechanical trauma
  2. Chemical trauma (caustics, etc.)
  3. Inflammatory trauma (peri-urethral abscess)

Thus underlying any nontraumatic diverticulum of the urethra in the male is an embryological deficiency which is aggravated by either obstruction, hormones, nerve injury, or any combination of these. Only in this way can we explain the rare appearance of diverticula under identical clinical and hydrodynamic conditions. The traumatic diverticula occur because of artificially induced weakness, the others occur from a basic embryological deficiency.

PATHOLOGY

Pathologically the normal transitional epithelium of the urethra is usually the seat of squamous metaplasia of varying degrees. The diverticulum wall is generally dense fibrous tissue of the compressed spongiosum which becomes atrophic.

SYMPTOMS

The congenital diverticula may be symptomless, as in case 1 of this paper. In infants, however, these diverticula may cause urinary obstruction with retention as reported by Gross et al.

In adults, infection within the diverticulum results in foul urine, frequency of urination, and stone formation within the sac. The most constant sign is the development of a midline mass which is fluctuant and empties on manual pressure. This mass enlarges during micturition and may cause delayed dribbling.

Final diagnosis is made by panendoscopy or cystourethrography.

CASE REPORTS

Case 1. E. D., a 27 year old white man, was seen because of bloody semen of 3 weeks' duration. Two months previously, torsion of the cord required orchiectomy. Examination revealed the absence of the left testicle, and a boggy and swollen prostate and seminal vesicles. The prostatoseminal secretion revealed microscopic pus and blood. A diagnosis of prostato-seminal vesiculitis was made and he was treated conservatively. When the inflammation subsided, panendoscopy disclosed an opening on the floor of the bulbous urethra. The opening measured 5 mm. in diameter and would not admit the sheath of the panendoscope. A cysto-urethrogram showed a diverticulum (fig. 1). The patient had never had a urethral infection or injury, and the urethra was patent to a 28F sound. The patient had been symptomless, and as a result, no definitive treatment for the diverticulum was administered.

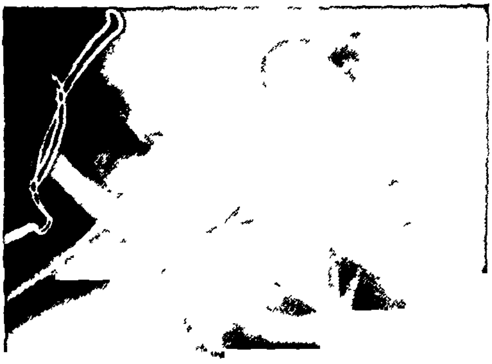

FIG 1. Case 1. Congenital asymptomatic diverticulum

This is an instance of a true congenital diverticulum in an adult without any history of any previous urethral obstruction. If, however, he should in the future develop strictures or require the use of a clamp, this diverticulum may well become clinically significant.

Case 2. M. F., a 59 year old white man, was first seen November 30, 1948 because of urinary retention and a previous history of prostatism. Examination revealed a firm but not stony hard prostate. A diagnosis of benign prostatic hyperplasia was made and a transurethral prostatectomy done on December 2; 35 gm. tissue was removed without incident. The postoperative course was uneventful. Examination of the tissue revealed low grade adenocarcinoma. Acid phosphatase both pre- and postoperatively was normal.

The patient was placed on 10 mg. stilbesterol daily, and on January 13, 1949 a total perineal prostato-seminal vesiculectomy was done. The postoperative course was uneventful save for a ten day period of perineal urinary fistula which closed spontaneously without a catheter.

At first the patient was totally incontinent of urine except when lying down or at rest. He was given sphincter exercises (alternate starting and stopping the stream). He was also given 10 mg. of stilbesterol daily. In order to allow his bladder to fill more fully during the day so that he could practice his sphincter exercises, he used a Cunningham incontinence clamp. This he used only while at business during the day which involved only eight to ten hours; at home he had no need for it. The incontinence diminished to stress incontinence of a minor degree.

FIG. 2. Case 2. Diverticulum that developed after surgery

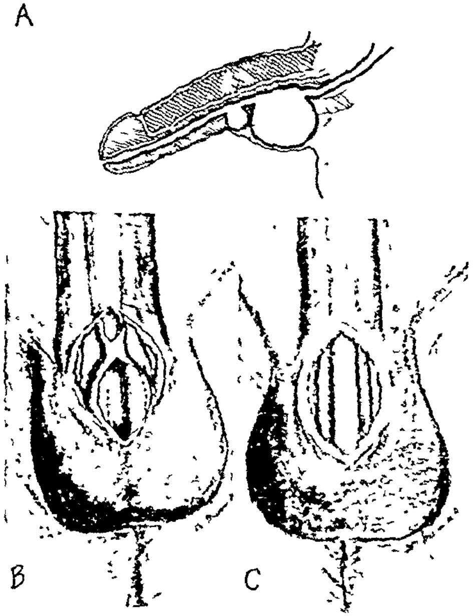

FIG 3 *A*, schematic drawing of long section of penis *B*, diverticulum opened with lines of incision. *C*, repaired urethral showing suture line on right side.

Three months after prostatectomy, the caliber of the urethra was 28F. Seven months after the total prostatectomy, a walnut sized mass was noted at the penoscrotal junction. It was not painful and collapsed on manual pressure causing urine to come out of the urethra. Panendoscopy showed no distinct opening, but there seemed to be a diffuse dilatation of the bulbous urethra. The use of the clamp was terminated, and the distal urethra dilated to 30F to afford free drainage. Stress incontinence continued and in spite of the removal of the obstructing clamp, the sac seemed to enlarge. A cysto-urethrogram on January 20, 1950 revealed a sacciform diverticulum of the bulbous urethra, and a smaller one distal to it on the pendulous urethra (fig. 2).

On February 7 a diverticulectomy and urethral repair was done.

The pathological change noted at operation was an epithelial lined bulging of the floor of the bulbous urethra for a distance of four centimeters with no change in the continuity of the roof of the urethra. A longitudinal schematic drawing is seen in figure 3, *A*.

The larger diverticulum had compressed and atrophied the corpus spongiosum and was separated from the skin by a much attenuated Buck's fascia and Colles' fascia.

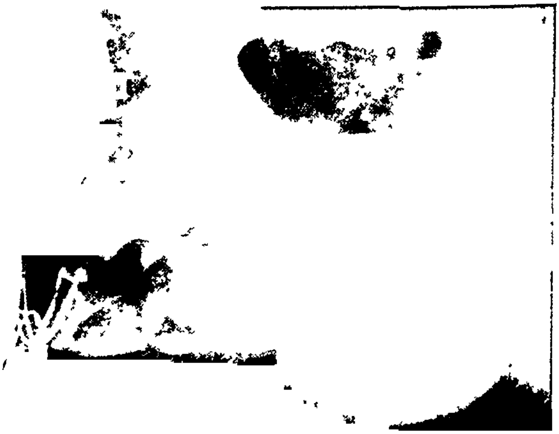

Fig. 4. Case 2. Postoperative cysto-urethrogram

TECHNIQUE OF REPAIR

A midline incision was made over the penoscrotal junction and the fascia of Colles incised. The diverticulum presented immediately into the wound covered by thin atrophic corpus spongiosum. This was incised and the larger diverticulum exposed. The diverticula was then opened and the redundant tissue on the ventral aspect resected so that more was removed from the right of the midline than from the left. Thus a flap was formed which when placed over the catheter from left to right formed a new floor of the urethra with an intact vascular supply on one side (fig. 3, *B*). The resultant fibromucosal suture line came to lie on the right side of the newly formed tube and near its dorsal wall (fig. 3, *C*). This was done to avoid a midline suture line which might be in continuity with the skin incision and thereby predispose to fistula formation.

The deep fascia was then closed with interrupted double "0" chromic catgut sutures, with a drain of rubber tissue down to the urethra. The skin was closed with silk interrupted sutures. The drain was left in situ 48 hours.

The catheter was left in situ for 3 weeks at which time the patient began to void around it. Upon removal, a urinary fistula developed through the previous site of the rubber tissue drain. This closed spontaneously in 9 days. The postoperative cysto-urethrogram taken on May 12 is shown in figure 4.

Immediately postoperatively (after the perineal fistula had closed) the patient was continent except on severe straining; at this time he had not had stilbesterol for 2 months. However, because of apprehension over recurrence of cancer, this medication was started. Two days afrer the institution of estrogen therapy, he became completely incontinent again. The dosage was reduced and the incontinence became a stress incontinence of a moderate degree. After 6 months it was completely discontinued and the continence returned as before therapy had been started, thus demonstrating the effect on muscle tonus of estrogens.

DISCUSSION

In the foregoing pages it has been postulated that the basic reason for any nontraumatic diverticulum of the male urethra is a congenital weakness of the urethral wall or a frank congenital diverticulum lying symptomless until distal obstruction of the urethra enlarged it making it clinically evident.

This theory has support in the work of Johnson on human embryos, and in the observations of the 2 cases in this paper where a symptomless congenital diverticulum was observed in an adult. This theory of congenital predisposition or actual herniation is readily explainable embryologically and is in keeping with similar ideas on the congenital predisposition to the formation of cystocele and inguinal hernia on the basis of embryologically poorly formed supporting structures.

The great mass of distal urethral obstructions (strictures and Cunningham incontinence clamps) occurring in everyday practice over prolonged periods of time would have certainly yielded many more instances of diverticula if back pressure alone were the sole factor in the formation of these abnormal structures.

In addition the influence of nerve injury as a contributory factor, as postulated by Fagerstrom, is considered and given its place as an etiological factor in the causation of diverticula. This increased susceptibility to diverticulum formation is amply demonstrated by the much higher incidence of diverticula noted in the series of Pate and Bunts collected in paraplegic patients who had peri-urethral abscess.

Furthermore, the relaxing effect of estrogenic substances on the smooth muscle and connective tissue is presented as a third factor which might contribute to the development of a diverticulum if congenital weakness were present. It is believed that in case 2, this, in addition to the previous two factors, led to the formation of the diverticula in question.

I believe, therefore, that whenever a Cunningham incontinence clamp is to be used, a cysto-urethrogram should be done to rule out any congenital diverticula which might be present and asymptomatic. This holds true especially if estrogens are to be used

SUMMARY

The literature has been reviewed and 2 cases of diverticulum of the male urethra added to it. This totals 235 cases reported in the extant literature.

The various theories of formation of non-traumatic diverticula are discussed.

The concept is advanced that all nontraumatic diverticula are due to embryologically incomplete or nonunion of the inferior surface of the urethra during fetal life.

The relaxing effect of estrogens on smooth muscle and connective tissue and its relaxation to development of diverticula is discussed.

The author wishes to gratefully acknowledge Dr. William A. Griesau's splendid drawings of the surgical procedure.

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THE CLINICAL PROGNOSIS IN TESTICULAR TUMORS: AN ANALYSIS OF 48 CASES

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Many excellent reviews of testicular tumor (Belt, Dean, Ewing, Friedman and Moore, Henline, Higgins and Bucker, Hinman, Lewis, Lowry, Ormond, Skully, and Tarner) as well as methods of treatment (Camberlain and Jamison, Kelby and Strenstrom, Leddy and Desjardins, Leuctia and Pendergass) are to be found in the literature. The general opinion at present as gleaned from these papers is that the prognosis in testicular tumors depends upon cell type and the use or lack of x-ray therapy. Barringer stated that the prognosis depended upon 1) pathological examination of the tumor, 2) determination of involvement of the cord, 3) physical examination of the patient, 4) distribution of lymph stream involvement, and 5) a thorough knowledge of autopsy material. The physical examination was just stated and not analyzed in relation to the prognosis.

Belt stated that early seeking of aid by the patient and early diagnosis by the doctor were essential for a good prognosis in testicular tumors. More than one-half of his cases who had symptoms for more than 5 months had metastasis. Sixty-five per cent with a history of 3 months or less were well for at least 3 years. He stated that the prognosis depended also on the presence or absence of metastasis and the radiosensitivity of the tumor.

Hinman summarized the prognosis in testicular tumors as:

1) Good: The patient is physically fit, there are no demonstrable metastases and the hormone has disappeared from the urine;

2) Fair: The patient is in good physical condition and the structure of the tumor indicates that it will respond well to x-ray therapy. However, metastases have appeared and the hormone persists even though low and diminishing under irradiation; and

3) Poor: The patient is losing ground physically; metastases resist treatment or rapidly recur and the hormone in the urine is little affected or even increases under radiation.

Desjardins, studying the importance of the retroperitoneal lymph nodes in relation to malignancy, noted significant symptomatology connotating a poor prognosis. Pain in the back and abdomen, bloating, belching after meals, abdominal distention, increase in flatus, a sensation of undue fullness after eating, gradual increase in size of the abdomen and constipation were indicative of metastasis to the retroperitoneal nodes.

Randall used the excretory urogram as a prognostic test with x-ray treated recurrent abdominal masses. Nonfunctioning kidneys due to obstruction by metastatic masses showed return of function and essentially normal pyelograms in those patients showing a good response to therapy.

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Ormond and Prince listed many of the chief complaints of patients with testicular tumors but did not evaluate these in relation to the end result. Pendergass evaluated two points in the history when he noted that lumbar pain and abdominal cramps with gastro-intestinal disorders were bad prognostic symptoms.

Gilbert in studying 7000 case reports of testicular tumors, stated that 1.5 per cent occurred in testicles of normal size or smaller. This did not, however, have any relationship to the prognosis, malignancy of the tumor or the presence or absence of metastasis. He noted a high incidence of chorio-epitheliomatous tissue with atrophy (8 of 46 cases). This later statement certainly would appear to be contrary to the previous one since the prognosis of chorio-epitheliomas is extremely poor.

Although the incidence of trauma in relation to tumors of the testis is quoted by various authors (Carins, Gordon-Taylor, Dean, Gilbert) as varying between 10 to 30 per cent, no mention is made of its relation to prognosis.

While the truth of these opinions is not in any way contended, it is believed that in applying them to any one case, many other modifying factors seem to be present. It was with the idea of analyzing these factors in relation to the prognosis of testicular tumors that this study was undertaken. An attempt was made to analyze the prognosis in relation to the various points noted in the history, physical findings, laboratory findings and treatment.

MATERIAL FOR STUDY

Fifty-two cases of testicular tumors have been treated in the period from 1926 to 1949. Forty-eight tumors were malignant and 4 were benign. The malignant tumors were placed in four basic classifications as advocated by Friedman and Moore; seminoma, embryonic carcinoma, teratocarcinoma and chorioepithelioma. Thirty-one cases were operated upon at this institution and 15 were operated upon elsewhere, having been referred here for x-ray therapy or seen here at the time of recurrence of their tumor. Two cases were not operated upon. A man, 27 years of age, entered the hospital with the chief complaint of weakness of his arms and died 6 days after admission. A clinical diagnosis of chorio-epithelioma based on his short history of 8 weeks and a high titer of hormone in the urine was confirmed at autopsy. The second case was that of a man, 35 years of age, who had been treated for 6 months for a migratory thrombophlebitis. Upon admission to the hospital, he was found to have a testicular mass, a mass in the left lower quadrant and a mass pressing in the region of the stomach. The Aschheim-Zondek test was positive and he died one month after discharge from the hospital. He was seen on the medical service and no x-ray therapy or surgery was carried out. Two cases underwent abdominal operations. Biopsy of the retroperitoneal mass in one case was diagnosed Hodgkin's disease. A review of the biopsy and autopsy slides during the present study revealed the correct diagnosis to be embryonic carcinoma of the testicle with metastasis to the retroperitoneal lymph nodes. The second case, likewise presenting a retroperitoneal mass, proved to be metastatic embryonic carcinoma from the testicle.

All deaths have been attributed to the testicular tumor. Although death apparently was due to coronary occlusion in two men, no autopsy was performed to confirm the clinical diagnosis. These deaths, therefore, have been considered as due to the original testicular malignancy.

HISTORY

The pertinent factors in the histories were tabulated. The number of cases noted in relation to the various points in the history are less than the total number of cases studied due to the inadequacy and incompleteness of the history in some instances. The symptom or complaint was tabulated only when the presence or absence of such symptom and complaint had been definitely stated. Thirty-five of the 48 cases occurred between the ages of 21 and 50. Fifty per cent of these are alive. Of the 13 cases occurring outside these age groups, 12 of whom were followed, only 2 are alive. Perusal of the chief complaint revealed that when it is related to the testicle the prognosis is better than when it is unrelated to the testicle. When no chief complaint was present and the testicular tumor was found incidentally on physical examination, 2 out of the 3 cases are alive. In the group presenting a history of pain, 20 per cent are alive as against 58 per cent without pain. Pendergass recognized lumbar pain as a serious complaint in 9 of 21 patients. Dean noted pain in 7 per cent of his cases but did not correlate it with survival time. A history of attacks of pain has essentially the same prognostic significance as pain itself. Of the patients with enlargement of the testicle which occurred gradually, 58 per cent are alive, but when acute enlargement or gradual plus acute enlargement occurred, only 31 per cent are alive. The interval since the onset of symptoms seems significant in that of those who waited more than a year before seeking treatment, only 1 out of 5 is alive while of those with a history of less than 1 year, 14 out of 30 are alive. The occurrences of weight loss carried a grave prognosis in that but 1 out of 7 is alive. A history of injury to the testicle was most interesting because it seemed to have brought the patient's attention to his condition. Gilbert, reporting on the investigation of the relation of injury to testicular tumors in compensation cases, stated it is not significant and the incidence of injury is as high or higher in benign enlargements. The incidence of trauma in the report of Nash, Carins, Gordon-Taylor and Dean range from 10 to 30 per cent. Out of 14 cases with a history of injury, 9 are alive, while 8 out of 23 without a history of injury are alive. Trauma may well call the patient's attention to an already existing testicular tumor which has been asymptomatic. Keifer expressed a similar opinion. The presence of tenderness showed a reduction in survival from 12 out of 22 alive without tenderness to 4 out of 11 with tenderness. A family history of carcinoma, present only in 7 out of 34, did not seem to carry any prognostic significance. Perusal of the average time of survival to death and the average length of time alive of the survivors up to the time of the present study, revealed a definite increase in many months survival time in the absence of these symptoms just discussed over the survival time when these symptoms are present.

PHYSICAL EXAMINATION

The side involved by the testicular tumor was right, 24 and left, 21, which corresponds to the relative incidence as quoted by Dean and Barner. The mass was usually described as stony, hard, firm, or tense. The description varied from patient to patient and from examiner to examiner in the same patient. There seemed to be no difference in the prognosis whether the tumor was confined either to the upper or lower part of the testicle or involved the entire testicle. With tumors having a regular contour, 7 out of 10 persons are alive compared with 7 out of 16 with an irregular contour. This point in the physical examination may be significant but the average time of survival is not consistent with such a conclusion at the present time. The physical examinations were not complete enough in order to evaluate the appearance of dilatations of the veins of the side involved or induration of the cord. From this study no prognostic significance can be given for these findings, but Powell showed that evidence of extension of the growth in the spermatic cord should give a poor prognosis. The presence or absence of palpable lymph glands other than the finding of a definite mass seemed to be of the most prognostic importance. Of the 28 patients without palpable lymph glands, 14 are alive while only 2 out of 7 with lymphadenopathy are alive. The 5 who succumbed were dead on the average within 10 months. All of the patients (six) who were found to have a palpable mass at the time of the original examination, died on an average in 9 months.

LABORATORY STUDIES

The usual laboratory studies were carried out. The white blood cell count and the urine examination were of no prognostic significance. The Aschheim-Zondek test (rabbit) performed in 23 instances revealed only 20 per cent survival when positive as against 61 per cent when negative (table 1). Owen and Cutter showed that the virgin rabbit test requires a minimum of 2000 m.u. to be positive. Twombly reported a 23 per cent mortality with less than 1000 units as against 57 per cent mortality with 1000–2000 units and 82 per cent with more than 2000 units. He felt that a positive Aschheim-Zondek test carried a grave prognosis. A similar opinion was expressed by both Smith and Powell. Alkaline phosphatase determination, gonadotrophins and 17-ketosteroid levels were carried out in some instances but were too few in number for any conclusions to be drawn. In 6 cases showing metastases to the lungs by x-ray, all were dead on an average within six and one-half months. Of the 21 showing no evidence of metastases, 15 are alive, an average of three and one-half years (table 1).

The pathological classification of the tumors showed almost 50 per cent to be embryonic carcinoma. We were unable to classify 4 of the tumors because the slides were not available for restudy. The survival rates according to type showed the extremely poor prognosis of the chorio-epithelioma and the good prognosis of the seminoma with embryonic carcinoma taking a middle position. Cabot and Berkson reported 75 per cent 5 year cures in seminoma and only 37 per cent in embryonic carcinoma. The over all survival, the deaths, and the patients alive to date are shown in table 2. Seventy-four per cent of those who

TABLE 1. *Laboratory findings and time survival*

A-Z TEST (23) CASES	DEAD	ALIVE	% ALIVE	AVERAGE TIME TO DEATH	AVERAGE TIME SURVIVAL
Positive, 5.	4	1	20	8 months	7 years, 9 months
Negative, 18	7	11	61	10½ months	4 years, 5 months

Positive:

Chorio-epithelioma—2—Dead.
Seminoma: (Met. embryonic carcinoma—1—Dead.
No operation or autopsy—1—Dead.
Embryonic carcinoma—1—Alive.

CHEST X-RAY (27) CASES	NO.	DEAD	AVERAGE TIME TO DEATH	ALIVE	AVERAGE TIME ALIVE	AVERAGE TIME FOR THOSE ALIVE MORE THAN ONE YEAR
Metastasis	6	6	6½ months	0		
No metastasis	21	6	10½ months	15	3½ years	4 years, 8½ months

TABLE 2. *Time distribution in years in relation to survival*

	YEARS						
	1	1–2	2–3	3–4	4–5	5–10	Over 10
Patients alive to date	5	2	2	0	2	6	2
Dead	13	3	4	1	2	3	1
Overall survival	18	5	6	1	4	9	3

TABLE 3. *Results of x-ray treatment*

X-RAY (31) CASES	OVERALL SURVIVAL					
Years	1	1–2	2–3	3–4	4–5	5
No. of cases	11	5	4	0	3	8

	Dead (14)					Alive (17)					
Years	1	1–2	3–4	4–5	5	1	1–2	2–3	3–4	4–5	5
No. of cases	6	3	2	2	1	5	2	2	0	1	7

NO X-RAY (13) CASES	OVERALL SURVIVAL					
Years	1	1–2	2–3	3–4	4–5	5
No. of cases	7	0	2	0	1	3

	Dead (10)						Alive (3)					
Years	1	1–2	2–3	3–4	4–5	5	1	1–2	2–3	3–4	4–5	5
No. of cases	7	0	1	0	0	2	0	0	1	0	1	1

succumbed died within 3 years. Of those patients alive, 52 per cent have been followed for over 4 years. The over all 4 year survival was 35 per cent. Kelby and Stenstrom reported a 29 per cent 5 year survival while Cabot and Berkson's over all 4 year survival was 44 per cent with a five year survival of 42 per cent. In

1922 Tanner reported only 5½ per cent 5 year cures with surgery alone and Hinman increased this to only 17 per cent with radical surgery.

TREATMENT

The results of x-ray treatment versus no x-ray treatment are shown in table 3. The over all survival with x-ray treatment is 55 per cent against 23 per cent without x-ray treatment. This is in agreement with the figure of 53 per cent over all survival as quoted by Leddy and Desjardins. With x-ray treatment, the most significant increase in survival time was noted with the seminoma and the teratoma. Chorio-epithelioma, as in the experience of others, carries essentially 100 per cent mortality. Taylor, however, reported a 9 year cure of a chorio-epithelioma. With x-ray treatment to metastatic lesions in 10 cases, 2 patients are alive an average of 6 years, 2½ months. This is in agreement with the findings of Leucutia who quoted 29 per cent, Cabot and Berkson 30 per cent, and Chamberlain and Jamison 17 per cent 5 year survival with the use of irradiation in metastatic tumors of the testis.

TABLE 4. *Prognosis in terms of symptoms, examination, x-ray therapy and laboratory studies*

GOOD	POOR
Chief complaint related to testicle	Chief complaint not related to testicle
No pain	Pain
Gradual enlargement	Enlargement acute or gradual plus acute
Interval less than 1 year since onset of symptoms or noticeable enlargement	Interval more than one year
No weight loss	Weight loss
History of injury	Finding incidental or accidental
No glands (+ inguinal)	Enlarged glands (+ inguinal)
No masses	Mass
Negative chest plate	Positive chest plate (Met.)
Seminoma	Chorio-epithelioma
X-ray treatment (adequate) At least 3–3500R Through 6 Ports	No x-ray treatment
Negative A-Z test	Positive A-Z Test
Between 20–50 years of age	Younger than 20 years, older than 50 years
No involvement of spermatic cord	Involvement of spermatic cord
? Regular tumor	? Irregular tumor

DISCUSSION

It is always difficult in any isolated instance of a malignant growth, to give a prognosis unless all the factors concerned are evaluated. While it is true that a seminoma of the testis on the average has a much better prognosis than other types, I believe that in an individual case the various points in the history and physical findings and the laboratory studies when coordinated will offer a better guide to the prognosis of the patient being evaluated. Surgical extirpation and adequate x-ray therapy when reviewed in relation to the other symptoms and findings have been tabulated in table 4. Examination of these points shows that some of them are common to tumors in general; namely pain, weight loss, metastatic involvement and rapid growth of the tumor. Others, however, are peculiar to testicular tumors: namely the chief complaint and history of injury, type of tumor (not grade of malignancy), contour of tumor and the Aschheim-Zondek test. While the use of x-ray therapy in increasing greatly the time of survival in malignant disease is not confined to testicular tumors, it is of such major importance in the consideration of the prognosis of testicular tumors that the lack of its use today is unpardonable. Of the 11 patients who have now survived more than 5 years, 8 received x-ray therapy and 3 did not. It is interesting to note that 6 were embryonic carcinomas, 3 were seminomas and 2 were teratocarcinomas, 26 per cent, 26 per cent, and 25 per cent respectively of the total number of each type in those classifications.

SUMMARY

I believe it has been demonstrated that in the individual case, many other factors besides the tumor type can be used in determining the prognosis of a person having a testicular tumor. These factors have been analyzed and enumerated

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ENDOTHELIOMA OF PENIS: A CASE REPORT

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As only 12 cases of this type of tumor have been reported in the literature, it is believed that the following case is of sufficient interest to warrant reporting.

A. F., a white man aged 41, was first seen by one of us (W. D. C.) August 1, 1948. At that time he complained of painful nocturnal erections which had been present for about a year. At first these occurred every two or three nights and later nightly with considerable loss of sleep. Recently they became so frequent that the patient obtained very little sleep and became run down and irritable. He had no pain during the day and no difficulty in voiding. A few days previously he had noted a small lump at the base of the penis. He was admitted to the hospital August 16.

Examination revealed a well developed, well nourished but rather pale individual. In the right inguinal region there was one large and two smaller glands. At the base of the penis and slightly to the right was a hard lump, about the size of a walnut. This was not attached to skin but was firmly attached to the underlying structures and surrounded the base of the penis. It was not tender on pressure. Cystoscopic examination was negative.

A biopsy taken August 19 consisted of four fragments of firm white tissue. Microscopic examination revealed no definite capsule but masses of low cuboidal cells growing within sinusoids. The greater part however, consisted of elongated cells with associated dense fibrous tissue. A diagnosis of malignant endothelioma, cavernous angiosarcoma was made.

On September 16 a radical amputation was done with removal of the superficial glands in the inguinal region and Scarpa's triangle. It was found that the tumor at the base surrounded the penis completely and involved both corpora cavernosa and corpus spongiosum. This was removed en masse from the tuber ischii and perineal membrane. The urethra was transplanted to the posterior of the scrotum. Following operation dilatation of the urethra was required three times. The patient was discharged on October 2.

Examination of the surgical specimen revealed a penis with several glands. The penis measured 11.5 by 3.5 cm. The glans and distal portion appeared normal. The skin of the proximal part was denuded exposing the corpora cavernosa and corpus spongiosum. On section no definite tumor was found but at the junction of the middle and proximal third the tissue cut with very marked resistance. Microscopic examination revealed a structure similar to that found in the biopsy.

From November 1 to 26, 1948 this patient received radiation directed to both inguinal regions, a tumor dose of 3000 r being given in both areas. Following this he carried on until July 1949 pain developed in the left hip radiating to the back of the thigh. He was weak and breathless and had lost a good deal of weight. X-ray examination revealed multiple infiltrative lesions in both lung fields from

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apex to base. From September 1 to 30 he received 3000 r directed to the chest. His condition deteriorated and he expired October 30, 1949.

Autopsy disclosed a massive recurrence in the region of the symphysis, with thick infiltration along the urethra to the urethral opening in the scrotum, gross infiltration of the inguinal glands, and scattered nodules throughout both lungs. No other metastases were found.

Microscopic examinations of these tissues demonstrated the true nature of the lesion. In the lungs large blood channels with proliferation of the lining endothelial cells to give large cells masses of extremely pleomorphic cells placed beyond doubt the nature of the tumor. The local recurrence and inguinal glands showed extensive necrosis.

SUMMARY

A malignant endothelioma, cavernous angiosarcoma, in a 41 year old white man, with fatal outcome in 13 months is described.

We should like to acknowledge assistance from Dr. W. L. Robinson, Banting Institute, Toronto for aid in making the original diagnosis. We are also indebted to Dr. A. C. Singleton, Department of Radiology, Toronto General Hospital, for details of radiotherapy.

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DISTORTION OF PYELOGRAM BY EXTRARENAL LESION: LIVER ABSCESS DISTORTION OF PYELOGRAM

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A pyelographic study of the kidney is a diagnostic aid and a great help in determining the extent and nature of renal diseases. In some instances, however, variations of the so-called normal pyelograms are deceptive and should be reported. These variations should be studied so that their proper significance is recognized when they are encountered at other times.

Within the past 3 years 3 cases in this hospital have presented certain similarities in history and symptoms, but all of which presented much difficulty in diagnosis and the true etiology was determined only at operation.

CASE REPORTS

Case 1—J. F. E., No. 57,160, a 31 year old white veteran was admitted to the Columbia V. A. Hospital, March 3, 1948, complaining of diarrhea, weakness and abdominal pain. He gave a history of having had fever and aching of extremities and loss of considerable weight during the preceding months. The history of his past illnesses was not especially illuminating except for an attack of frequency of urination while in service in England in 1945, and gonorrheal urethritis in 1946. On admission the patient's appearance was that of chronic illness and dehydration. He was pale and appeared anxious. The blood pressure was 130/84 and the examination of the heart and lungs revealed no abnormality. His abdomen was somewhat distended and a generalized spasm of the abdominal muscles was noted, most marked on the right side. There was indefinite right costovertebral angle tenderness and the liver appeared slightly enlarged. Examination of the urine showed 25–30 red blood cells per high power field and 15–20 white blood cells per high power field. The blood picture showed a white blood count of 12,000 and a red blood count of 3,400,000, with a hemoglobin of 55 per cent. A cystoscopy was done as part of our examination and the retrograde pyelogram showed what was thought to be a filling or pressure defect in an enlarged right kidney (fig. 1). The preliminary diagnosis was either a renal tumor or carbuncle. After a period of supportive treatment, including several transfusions, and a course of penicillin, the blood picture had changed to 5,000,000 red blood cells and 97 per cent hemoglobin. Exploratory operation of the right kidney was performed on March 18, 1948. A lumbar incision was made and a large normal appearing kidney was exposed. A very markedly indurated mass was palpated anterior and apparently superior to the kidney. This was determined to be an intrahepatic abscess and was drained extraperitoneally, releasing approximately 1000 cc of thick yellow pus. The patient experienced a

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smooth and comparatively rapid convalescence and follow-up intravenous pyelograms showed a restoration of the renal pattern to normal.

Case 2.—J. W. M., No. 68,732, a 27 year old white man, entered the Columbia Veterans Administration Hospital on January 11, 1949 with pain over the right costovertebral angle. He gave a history of previous severe right costovertebral angle pain and hematuria while doing guard duty at Oak Ridge. He was hospitalized at that time for 19 days and improved on sulfa therapy. The past history revealed that he was a patient in this Veterans Administration hospital in 1947 for a hemorrhoid operation and at that time was found to have a nonspecific prostatitis. Two days before coming to the hospital for the present admission, he noticed soreness in his right side which persisted, even after rest in bed. On admission it was noted that the patient showed evidence of abdominal tenderness extending into his right lower chest and costovertebral angle. He also complained of frequency and urgency of urination, but no hematuria was observed. The urologic examination on admission pointed to right renal disease and cystoscopy with retrograde study was done on the fourth day. The pyelographic x-ray reading was as follows: "On the right there is a moderate degree of dilatation of the renal pelvis and calyces." He was then seen by a medical consultant who diagnosed a respiratory infection complicating intra-abdominal disease. Daily chills were recorded associated with temperature of approximately 103 degrees. Repeated white blood counts varied from 6–9,000. Six days after admission an x-ray examination of the chest revealed a "moderate sized area of pulmonary consolidation at the extreme base of the right lung with pleural reaction". Repeat x-ray examination two days later revealed presence of fluid in the right pleural cavity. By aspiration, 50 cc of clear fluid was removed followed by rapid improvement in symptoms. On the seventeenth day after admission the temperature became normal and the patient was gaining weight. On the twenty third day after admission the radiologist reported from a study of

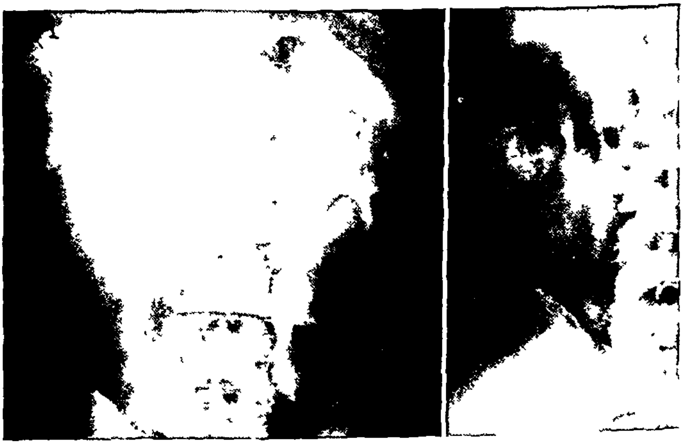

FIG. 1. Case 1 *A*, preoperative pyelo-ureterogram showing pressure defect on lateral pelvis, upper and middle calyces. *B*, postoperative excretory urogram Restoration to normal.

a gastro-intestinal series that the patient "had a mass in the right side extending down to the iliac crest and displacing the duodenal bulb to the left." The patient requested and was given leave for 2 weeks and on return complained of the same pain in his back to the right of the midline about the level of L-1. A week after his return from leave he again began having daily temperature elevations.

On March 4 and 5, more than seven weeks from the beginning of the first admission to the hospital, urologic study was again carried out. A "cut-off" appearance of the ureteropelvic junction was noted, probably due to an aberrant vessel, and also it was noticed that the right kidney was fixed in a very high position . . . and that the calyces were somewhat blunted (fig. 2). In our urology report we stated that "this picture suggests an old congenital malformation with also slight hydronephrosis, but this would not account for the present symptoms. The fixation of the kidney is very suggestive of an abscess or an inflammatory reaction nearby, but the process does not seem to be primarily intra-renal."

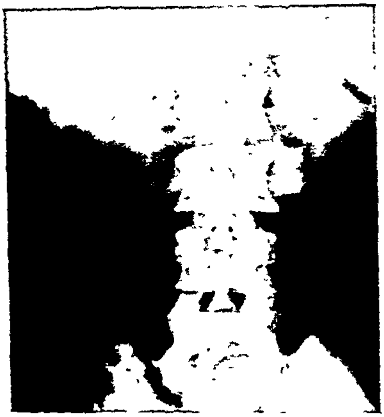

FIG. 2. Case 2. Preoperative pyelo-ureterogram showing pressure obliterating calyces. Right kidney fixed in position more medial and higher than opposite side.

Five days after the aforementioned cystoscopic examination an exploratory laparotomy was performed. On the undersurface of the liver a soft protruding mass the size of a man's fist was noted. On attempting to free this, an abscess was broken into which drained a thick yellowish red sticky material. Culture and smear were made from this and it was found to contain motile Endamoeba histolytica.

A postoperative excretory urogram showed that the position of the right kidney was now within normal limits. The pyelographic findings were essentially normal.

Case 3.—T. W. P., No. 70.980, a 30 year old white man, was admitted to the Columbia Veterans Administration Hospital on April 11, 1950. This World War II veteran had not been overseas and was discharged because of his "nerves." He stated that 6 weeks before admission he had influenza and has had dull to sharp shooting pains in the right costovertebral angle, which also radiated down the right flank and across to the suprapubic region lasting since the onset of his recent illness. No history of hematuria or pyuria was secured, but the patient had had fever several times and he was told by a urologist that he had a blood vessel obstructing the right kidney.

The physical examination showed a well developed and poorly nourished, asthenic 30 year old white man who appeared older than his age and also chronically ill. The examination was negative except for moderate tenderness and minimal muscular tension guarding the right costovertebral angle and the flank. There was a positive Murphy punch sign present.

On April 12 the urine showed 2-4 white blood cells, specific gravity 1.012 and he had a white blood count of 11,500, with 79 per cent polys, 4,600,000 red blood cells and 90 per cent hemoglobin. Kahn test was negative and blood urea nitrogen 12.3. A pyelogram of April 15 was reported "left normal, dilatation of the right with evidence of ureteropelvic obstruction." (fig. 3, *A*) The cystoscopic examination was negative except for small specks of whitish material coming from the right ureteral orifice and difficulty noted in advancing the right ureteral catheter past the right ureteropelvic junction. A 6F catheter was passed and was left in for drainage. Culture of urine yielded Staphylococcus aureus from the right and left pelves and bladder.

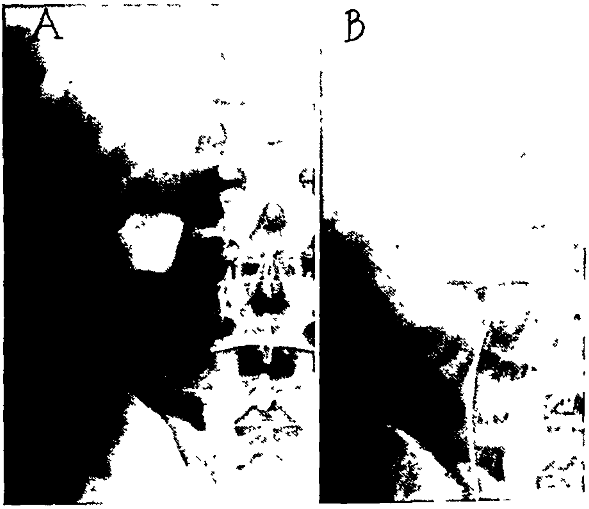

FIG. 3. Case 3. *A*, preoperative excretory urogram showing hydronephrosis, "cut off" appearance of ureteropelvic region and also pressure defect of upper lateral structures *B*, postoperative retrograde pyelogram showing satisfactory ureteropelvic repair and satisfactory filling of upper calyx.

April 26, the patient was anesthetized with pontocaine spinal anaesthesia and the right kidney exposed. It was adherent in the region of the upper pole, and the pelvis and upper ureter. These latter adhesions held the ureteropelvic portion of the ureter in an "S" shape, with an accentuation of the angulation when the kidney descended. The pelvis was enlarged and extrarenal. The upper ureter was dissected and the plication of the upper ureter was freed. A nephrostomy was done, draining a lower calyx. A 10F rubber catheter was used to drain the pelvis and an 8F ureteral catheter was passed down the ureter as a splint.

Following operation patient improved. The temperature which had been rising to 102 degrees showed signs of regression to normal. A normal temperature was maintained for 1 10-day period, when the temperature again rose to 102F. The white blood count at this time was 19,800 with 77 per cent polymorphonuclears. A mass, mostly anterior, developed in his right upper quadrant. A laparotomy exposed a liver abscess from which 1700 cc of thick chocolate brownish fluid was released.

Motile amoebae were not found in the wall of the abscess or in the pus at the time of operation, but were found in the pus 10 days later.

DISCUSSION

The 3 cases presented are similar in that they show recurrent acute episodes of right upper abdominal pain, with fever, and all had evidence of a pressure deformity of the pyelogram due to the disease within the liver.

It is difficult to explain how a swelling of an intra-abdominal organ would affect the shape of the calyces or pelvis of a freely movable kidney.

The upper peritoneal reflection, posterior to the liver, is higher than the upper pole of the kidney and as long as this peritoneal retrohepatic fossa is not obliterated by inflammatory change, pressure on the kidney from an intrahepatic mass would not be constant enough to deform the pyelographic pattern, but might tend to displace the kidney. When the space is obliterated and the liver and kidney become a part of one mass, then the pressure from the growth of the inflammatory mass would cause the deformities noted in these pyelograms.

The first case was approached from the flank and we had an opportunity to determine that while the abscessed liver and attached peritoneum could be displaced anteriorly in freeing the kidney, there were definite common adhesions between them. The other two cases were exposed through an anterior incision so the amount of adhesions between the kidney and posterior surface of the peritoneum could not be demonstrated.

All of the cases retained the psoas shadow to some extent, so a diagnosis of perinephritic abscess was untenable. All showed marked infection signs and symptoms, but with the first case we considered this was not incompatible with a diagnosis of hypernephroma or carbuncle. One had pneumonitis with pleural effusion. The urine of the first two showed definite pathologic findings consisting of many white blood cells and red blood cells. The third case was complicated by hydronephrosis from a tortuous narrowed ureter.

CONCLUSION

An abscess of the right lobe of the liver can cause definite urinary symptoms and can cause deformities of the pyelographic pattern. This occurs probably by the kidney first becoming adherent to the increasing hepatic abscess mass. When examining any patient with a painful condition of the right upper abdorecent illness. No history of hematuria or pyuria was secured, but the patient had had fever several times and he was told by a urologist that he had a blood vessel obstructing the right kidney.

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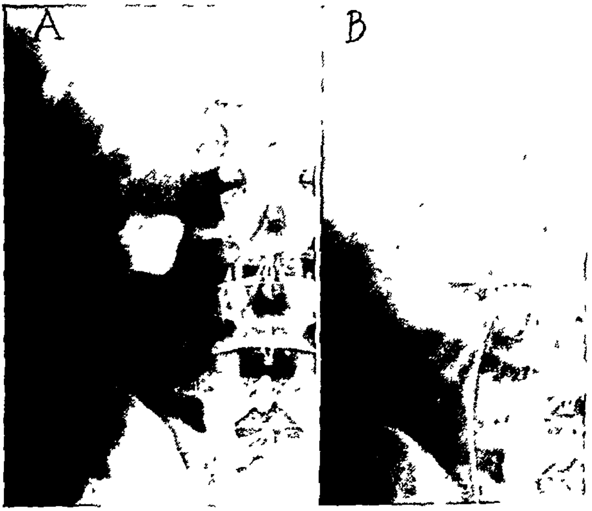

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CONCLUSION

An abscess of the right lobe of the liver can cause definite urinary symptoms and can cause deformities of the pyelographic pattern. This occurs probably by the kidney first becoming adherent to the increasing hepatic abscess mass. When examining any patient with a painful condition of the right upper abdomen, accompanied by fever, even though pyelographic changes are noted, one should keep in mind the possibility that the etiologic factor may arise in the liver.

Dr. Coppridge recently has reported a case of similar nature that was encountered in his clinic.

SUMMARY

Three cases of proven liver abscess are reported, all of which simulated primary renal disease. A theory is advanced to explain these pressure changes of the pyelographic pattern.

The author wishes to express his appreciation of the advice and assistance given by Dr. Karl Morgan Lippert, chief of surgical service, and Dr. Henry Potozyky, radiologist of this hospital.

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URINARY INFECTIONS: CLINICAL AND BACTERIOLOGICAL CURE WITH TERRAMYCIN

HOWARD M. TRAFTON AND HOWARD E. LIND, PH.D.

From the Brooks Hospital and the Sias Research Laboratories, Brookline, Mass.

The general practitioner and urologist are confronted with the increasingly complex problem of best treating urinary tract infections. This is due not only to the rapidly expanding number of available antibiotics, but also to the increase in bacterial resistance as well as patient intolerance to the drug. Urinary infections may be simple, mixed, recurrent or complicated by urologic lesions, such as obstruction or calculus formation. Instead of subjecting the patient to numerous costly medications which may not obtain permanent cure, it is felt that it is better to take a long range viewpoint and obtain complete bacteriological data at the onset, so that one or more antibiotics may be used to the best advantage.

Laboratory characterization of bacteria isolated is not sufficient for the evaluation of their pathogenic role.[1] Insufficient emphasis has been placed upon the significance of urologic lesions as factors in the prevention of ultimate cure. Also "in vitro" sensitivities have not been adequately interpreted in terms of clinical response.[2, 3, 4] This has been due to the lack of adequate bacteriological facilities in many hospital laboratories as well as the unavailability of accurate, rapid and inexpensive sensitivity tests. Refinement and standardization of the disc method for determining sensitivities has removed this latter obstacle. Physicians should be encouraged to use these tests routinely.

Preliminary work with terramycin had shown effectiveness against a wide spectrum of gram positive and gram negative bacteria associated with urinary infections. Tolerance had been generally good and few serious reactions had been encountered.

PROCEDURE

Thirty-five patients in this study were selected because the majority of these had failed to respond to sulfonamides and several other antibiotics including streptomycin, aureomycin or chloromycetin. Twenty-three males had a genitourinary tract infection with or without an additional nonspecific prostatitis, and 12 females had simple urinary tract infections. All patients received a complete urologic work-up to rule out the presence of obstruction and foreign bodies (calculi). This included cystoscopy and pyelography as a minimum, with urethroscopy or urethrograms as indicated. Prior to the initiation of treatment, urine cultures taken aseptically were submitted to the laboratory for isolation of microorganisms. Those isolated were tested for sensitivity against several antibiotics including terramycin, a procedure which normally takes 48 hours. Gram positive organisms were routinely tested for sensitivity against penicillin, aureomycin, and terramycin, and gram negative organisms against streptomycin, chloromycetin and terramycin. Results were reported as sensitive, moderately sensitive or resistant rather than in terms of definitive units. Repeat cultures were submitted for sensitivity determination on the third and seventh days of terramycin therapy as well as on follow-up examinations when catheterized urine sediment showed continued pus or bacteria.

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[1] Shwartzman, G.: Advances in the diagnosis of bacterial infections. Bull. New York Acad. Med., 26: 617, 1950.

[2] Herrell, W. E., et al: Terramycin: Some pharmacologic and clinical observations. Proc. Staff Meetings Mayo Clinic, 25: 183, 1950.

[3] Welch, H., Hendricks, F. D., Price, C. W. and Randall, W. A.: Comparative, studies on terramycin and aureomycin antibacterial spectrum, serum concentrations and urinary excretion. J. Am. Pharm. Assoc. Sc. Ed., 39: 185, 1950.

[4] Keefer, C. S.: Evaluation of antibiotic therapy. Postgraduate Medicine, 9: 101, 1951.

COURSE OF THERAPY

Most of these cases received 2 gm. terramycin* daily (2 capsules q.i.d. for 6 days). This dosage was selected on the basis of our previous experience with aureomycin and chloromycetin in similar urinary infections and proved to be generally adequate. Although there was frequent bacteriologic sterility after 3 days therapy, terramycin was continued for 6 days in order to prevent recurrence. A few patients with chronic urinary infection associated with non-correctable uropathy were able to remain symptom-free for long intervals on maintenance dose of 2–3 capsules daily.

REACTIONS OR DRUG TOLERANCE

Terramycin was found to be better tolerated than aureomycin, about the same as chloromycetin but less than penicillin or streptomycin. Some degree of diarrhea was present in about 36 per cent of those under treatment, but in most cases was not sufficiently severe to interrupt treatment. In addition, the patients frequently complained of other minor intestinal symptoms such as flattulence, gaseous indigestion resulting in loss of appetite and with an occasional unpleasant metallic taste in the mouth. In 2 cases acute sterile pharyngitis and glossitis was seen. Infrequently abdominal pain and weakness were encountered. Such mild intolerances, however, did not seem to diminish the clinical effectiveness of the drug. See table 1.

RESPONSE TO THERAPY

In the group of uncomplicated urinary tract infections 74 per cent showed complete bacteriologic cure following a single course of terramycin. An additional 10 per cent showed clinical improvement although subsequent cultures showed the continued presence of bacteria. Mixed or complicated urologic infections generally failed to respond to a single course of terramycin but did show clinical improvement with combined streptomycin-terramycin therapy. It seemed logical to combine streptomycin with terramycin in order to maintain an alkaline urine, a condition which is necessary for the most effective use of streptomycin, that is, to retard the development of bacterial resistance. This is difficult to maintain when aureomycin is used in combination.

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* Terramycin in 250 mg. capsules was furnished through the courtesy of Charles Pfizer Co., Brooklyn, N. Y.

From 35 patients, 56 micro-organisms were isolated, of which 28 were gram negative and 28 were gram positive. Initially, before therapy, 70 per cent were sensitive to terramycin "in vitro" (Difco Sensitivity Disc*). Of the gram negative organisms, 79 per cent were sensitive while Proteus sp. accounted for 66 per cent of those that were resistant. Of the gram positive organisms 61 per cent were sensitive while Micrococcus pyogenes var. aureus (hemolytic and nonhemolytic) accounted for 91 per cent of those that were resistant. In general it was found that among the gram negative organisms, excluding Proteus sp., greater than 90 per cent were sensitive to terramycin; among the gram positive organisms excluding hemolytic Micrococcus pyogenes var. aureus, greater than 80 per cent were sensitive. See table 2.

TABLE 1. *Drug tolerance in relation to clinical cure in 35 patients*

TYPE	REACTIONS*	CLINICAL CURE† Yes	CLINICAL CURE† No
Diarrhea	12	6	6
Rectal	6	3	3
Nausea	4	1	3
Gaseous indigestion	3	3	0
Glossitis and pharyngitis	2	1	1
Abdominal pain	0	0	0
Weakness	0	0	0

* Frequently more than one type of reaction appeared in same patient.
† 20 or 70 per cent of patients showed clinical cure.

TABLE 2. *Incidence and sensitivity of micro-organisms*

	GRAM NEGATIVE ORGANISMS S*	GRAM NEGATIVE ORGANISMS MS*	GRAM NEGATIVE ORGANISMS R*	GRAM POSITIVE ORGANISMS S*	GRAM POSITIVE ORGANISMS MS*	GRAM POSITIVE ORGANISMS R*
Pseudomonas aeruginosa	3	2	2			
Aerobacter aerogenes	4					
Escherichia coli	8	5				
Proteus sp.			4			
Micrococcus pyogenes var. aureus					3	6
Hemolytic micrococcus pyogenes var. aureus						4
Micrococcus pyogenes var. albus				3		
Enterococcus				5	6	1
Total	15	7	6	8	9	11
Percentage		79%			61%	

* S—sensitive—to 10 mcg.; MS—moderately sensitive—to 30 mcg.; R—resistant—to 60 mcg.

Repeat bacteriological examinations of urine cultures subsequent to initiation of treatment provided a means of comparing clinical cures with laboratory find-cultures taken aseptically were submitted to the laboratory for isolation of microorganisms. Those isolated were tested for sensitivity against several antibiotics including terramycin, a procedure which normally takes 48 hours. Gram positive organisms were routinely tested for sensitivity against penicillin, aureomycin, and terramycin, and gram negative organisms against streptomycin, chloromycetin and terramycin. Results were reported as sensitive, moderately sensitive or resistant rather than in terms of definitive units. Repeat cultures were submitted for sensitivity determination on the third and seventh days of terramycin therapy as well as on follow-up examinations when catheterized urine sediment showed continued pus or bacteria.

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	S*	MS*	R*	S*	MS*	R*
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Aerobacter aerogenes	4					
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Proteus sp.			4			
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* S—sensitive—to 10 mcg.; MS—moderately sensitive—to 30 mcg.; R—resistant—to 60 mcg.

Repeat bacteriological examinations of urine cultures subsequent to initiation of treatment provided a means of comparing clinical cures with laboratory findings. In general with the few exceptions previously cited there was good correlation between prognosis based on sensitivity tests and actual response. See table 3.

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* Terramycin discs were standardized by the tube dilution method against sensitive organisms.

Several points of interest are present in table 3. Although the presence of Proteus sp. and hemolytic Micrococcus pyogenes var. aureus suggested a poor clinical prognosis, there was marked improvement after a single course of Terramycin therapy. Frequently M. albus was found in mixed infections but this also disappeared following a single course of treatment. With other organisms present in mixed infection, when one of the several organisms isolated was cleared from the urinary tract, Terramycin failed to induce bacteriological cures on the remainder, particularly Pseudomonas aeruginosa and Micrococcus pyogenes var. aureus, although clinical improvement was marked.

TABLE 3. *Correlation between "In vitro" sensitivities and clinical and bacteriologic cures*

	INCIDENCE	INITIALLY SENSITIVE	CLINICAL CURE	BACTERIOLOGICAL CURE (BACT. STERILITY)
Ps. aeruginosa	7	5	6	4
A. aerogenes	4	4	4	4
E. coli	6	6	5	5
Proteus sp.	4	0	3	2
M. aureus	5	3	5	5
Hemo. M. aureus	4	0	2	1
M. albus	12	12	10	9
Enterococcus	8	8	7	7
Total	50	38	42	37
Percentage	100%	76%	84%	74%

DISCUSSION

In this study an attempt has been made to correlate initial bacterial sensitivity of a micro-organism with response to terramycin, clinically and bacteriologically. The importance of initially isolating the presence of microorganisms of known sensitivity cannot be overstressed: 1) to determine whether the urinary infection is simple or mixed, 2) to determine whether an urologic consultation may be necessary, and 3) to determine the most economical approach in treatment. Terramycin, because of its wide bacterial spectrum, was run against both gram negative and gram positive organisms. By the disc sensitivity method the majority of the gram positive organisms responded to penicillin, aureomycin, or terramycin, while most of the gram negative organisms showed sensitivity to streptomycin, chloromycetin or terramycin. In general, urine and blood levels for sensitivity as an indication to response to terramycin are of questionable value since in many instances those showing low blood levels responded equally as well as those indicating high levels.

During the interval pending sensitivity reports, a sulfonamide may be used if tolerated and the infection not already been found to be refractive. Streptomycin-terramycin combined therapy may be warranted in mixed infection or where bacterial sensitivity is only moderate.

SUMMARY

Terramycin is an effective antibiotic for treating many urinary infections caused by both gram positive and gram negative organisms, and has cured where all other antibiotics have failed.

Terramycin is generally well tolerated, the percentage of relapses being low and the percentage of bacteriological as well as clinical cures high.

In this series terramycin was found to be generally ineffective against Proteus sp. and certain strains of hemolytic Micrococcus pyogenes var. aureus.

Sensitivity discs can be used routinely with satisfactory results. They give the physician a fairly reliable guide to prognosis when selecting an antibiotic.

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A SIMPLIFIED PROSTATIC PERINEAL BIOPSY PUNCH

RALPH J. VEENEMA

From the College of Physicians and Surgeons, Columbia University and the Squier Urological Clinic, Presbyterian Hospital, New York, N. Y.

A simple and satisfactory instrument with which to biopsy all parts of the prostate gland is still being sought by urologists. During the past year at the Squier Urological Clinic, a new biopsy instrument has been used with satisfaction. It is a modification of the Gusberg endocervical biopsy curette[1] which has been adapted for perineal prostatic punch biopsy.

The tip of the instrument (fig. 1), 1.5 cm. in length, has biopsy cups 0.5 cm. in diameter. Clean globular bites of tissue averaging 0.3–0.4 cm. in diameter were obtained without distortion from crushing or burning. The tissue was large enough to permit a pathological diagnosis to be made on both cellular detail of the prostatic acini and stromal invasion. The size of the biopsies was entirely sufficient for pathological diagnosis and was not so large as to invite complications from the procedure itself. On our patients both frozen sections and the permanent hematoxylin-eosin stained sections have shown completely satisfactory diagnostic biopsies (fig. 2, *A*).

The procedure is not difficult and can be done on any office-type examining table, under pentothal, caudal or local anesthesia. With the patient in the lithotomy position, the perineum and genitalia are washed thoroughly and prepared with merthiolate. Sterile drapes are applied to leave both the perineum and genitalia exposed. The index finger of the gloved hand is lubricated, inserted into the rectum and the suspicious area located. If the prostate is high and a nodule difficult to reach, a sound is inserted by an assistant to depress the prostate towards the perineum. This is seldom necessary. A small stab incision is made in the perineal skin, to the right or left of the midline, depending upon the location of the nodule. The tip of the biopsy instrument is then inserted with the other hand, with the biopsy cups closed. The tip is first directed slightly anteriorly to avoid the rectal reflection and then, guided by the finger in the rectum, it is directed cephalad toward the prostate. The fusiform tip of the instrument may be readily palpated and is kept close to the rectal wall to avoid the vascular penile bulb. Definite resistance is met at the prostatic capsule and affords an opportunity to evaluate accurately, with the rectal finger, the proximity of the biopsy cups to the area of suspected carcinoma. A direct path is then taken to the area to be biopsied. When the instrument is within this area or adjacent to it, the biopsy cups are opened with the thumb and index finger. The hilt of the instrument is depressed slightly to encompass more tissue within the cups, and the biopsy cups closed. Pressing the nodule toward the opened cups with the rectal finger also aids, at times, in obtaining a larger biopsy. After closure of the cups the rear cup is rotated so as to cut off any strands of tissue holding the biopsy. The punch is withdrawn with the biopsy cups remaining

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[1] Gusberg, S. B.: Am. J. Obst. & Gynec., 57: 752, 1949.

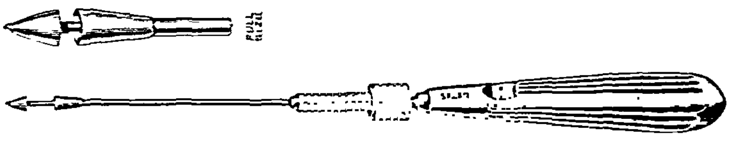

FIG. 1. Fusiform tip consists of two conical biopsy cups. Distal cup measures 0.5 by 0.5 cm. and the proximal cup, 1.0 by 0.5 cm. Tip is sharp and readily penetrates prostatic capsule. Instrument has a handle which can be firmly held in one's hand. Opening and closing of cups is done with thumb and forefinger which grasp knurled disc on shaft controlling rear cup. Biopsy cups can be opened 1 cm. and take clean globular bites 0.3 to 0.4 cm. in diameter.

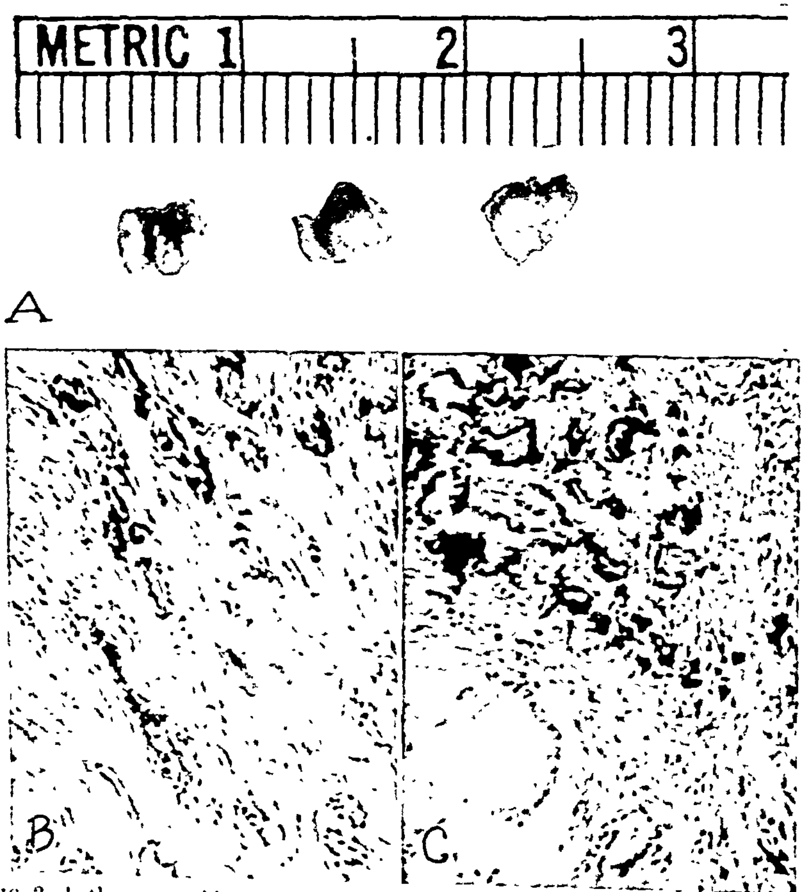

FIG. 2. A, three gross biopsy pieces. B, biopsy section showing prostatic carcinoma invading prostatic capsule and periprostatic tissue. C, area of carcinoma adjacent to benign prostatic acini.

closed. Bleeding is usually minimal and is readily controlled by perineal pressure for a few moments. The perineal stab incision is closed with one suture of plain catgut. Small toothed forceps are used to remove the biopsied tissue from the cups.

The biopsy punch was at first considered to be particularly indicated, to obtain, in a simple manner, histological proof of carcinoma when the diagnosis was quite definite by palpation. With its further use it became evident that small suspicious areas within the prostate could be accurately biopsied. At the Squier Clinic the punch biopsy has proved suitable for the selection of cases for retropubic total prostatovesiculectomy.

DISCUSSION

Prostatic biopsy in the manner described is a simple adjunct to diagnosis of prostatic nodules. Early prostatic carcinoma can be diagnosed by accurate biopsies; however, a negative punch biopsy certainly does not rule out carcinoma. In two of our cases subsequent open perineal exposures and open biopsies of the suspicious areas of carcinoma confirmed the punch biopsy diagnosis of benign prostatic hypertrophy. In all cases of prostatic carcinoma, even when obvious clinically, histological evidence of the disease is desirable when cases are to be evaluated statistically.

The risk of dissemination of tumor cells is no greater than with any other type of biopsy of a neoplasm. The efficacy of androgen-control treatment for prostatic carcinoma makes biopsy of prostatic lesions less hazardous than biopsy of other neoplasms.

SUMMARY

A new instrument for perineal prostatic punch biopsy has been reported. The fusiform cup-like biopsy tip permits ready palpation by the rectal finger, with increased accuracy of biopsy. The average diameter of over 50 biopsies done to date has been 0.3 – 0.4 cm. Tissue obtained was sufficient for pathological diagnosis and was not so large as to cause complications from the biopsy procedure.

I wish to express my appreciation to the J. Sklar Manufacturing Co. for their cooperation in developing the instrument; to Drs. George F. Cahill, Saul B. Gusberg, and John K. Lattimer, for their advice and assistance; and also to Dr. Meyer M. Melicow for review of pathological specimens.

THE JOURNAL OF UROLOGY
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A NEW DRAIN

FRANCIS A. BENEVENTI

From the Department of Surgery (Urology), Cornell University Medical School, New York, N. Y.

The purpose of this short paper is to present a new drain (fig. 1). It is simply a rubber drain (Penrose or other) with measured markings which serve to indicate to the surgeon what portion of the drain remains in the wound. Its use is appreciated during the postoperative course when it becomes desirable to shorten the drain without having it drop out of the wound. In shortening an ordinary drain, the surgeon has no way of knowing exactly how much of it remains in the wound; he can only guess.

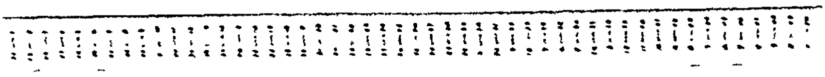

FIG. 1

The drain which is being presented has markings similar to those of a tape measure indelibly stamped in 5 cm. intervals throughout its entire length. By pulling a gauze strip through its lumen, it can be converted into a calibrated cigarette drain.

The drain is especially useful in retropubic and kidney surgery, but its usefulness in all branches of surgery is at once obvious. The need for such a drain first became apparent to me during the course of dressing the wound of a patient on whom I had done an operation on the kidney pelvis. I had shortened the drain several times and with the intention of further shortening it on the occasion of this dressing, I had unintentionally removed the entire drain.

As simple as this measured drain is, I have not seen anything similar to it, nor have I come upon it in the literature. I wish to thank Mr. Frederick J. Wallace of American Cystoscope Makers, Inc., who has always been eager to encourage new ideas and who has displayed it at annual meetings of the American Urological Association in Chicago in May 1951, and at the American Medical Association in Atlantic City in June 1951.

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The list of officers and members of the executive committees of the Sections and Branch Societies of the American Urological Association will be found on pp. 960-962, December 1952 issue

THE JOURNAL OF UROLOGY
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SOME PROBLEMS OF TESTICULAR FUNCTION

WARREN O. NELSON

From the Department of Anatomy, University of Iowa College of Medicine, Iowa City, Iowa

On this occasion I should like to consider three problems relating to the functions of the testis. In selecting these from the many problems which presently confront us I have singled out one which possesses a purely endocrine basis, one which has certain endocrine aspects but which almost certainly has other equally important facets, and one in which the endocrine component probably is insignificant.

The three problems in the order in which I should like to present them are:

1) The testis in hypogonadotrophic eunuchoidism.
2) The fate of the germ cells in the undescended testis.
3) Germinal cell or spermatogenic arrest.

In each of these problems recent observations have provided us with a certain degree of understanding of the defective process, but in none may we feel confident that our knowledge is sufficient to serve as more than sign posts for further study.

THE TESTIS IN HYPOGONADOTROPHIC EUNUCHOIDISM

This condition is one in which the testes fail to undergo maturation during the usual puberal years and failing suitable treatment remain permanently in an infantile state. The lack of testicular maturation usually is complete, i.e., spermatogenesis fails to occur and Leydig cells are not differentiated. As a result of the latter defect the testes do not produce androgenic hormone and the individual exhibits the classic stigmata of hypogonadism: small genitalia, absent or very scanty pubic, axillary, facial and extremity hair, eunuchoidal body proportions and a voice of feminine pitch.

It is important at this juncture to indicate that the physical complex described above is that of a eunuchoidal individual and not exclusively characteristic of the particular syndrome which occupies our immediate attention. Indeed, two other testicular defects result in similar physical pictures. These are puberal seminiferous tubule and Leydig cell failure or the eunuchoidal variant of the

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Read at annual meeting American Urological Association, Atlantic City, N. J., June 26, 1952.

The studies described in this paper have received support from a research grant (RG 1778) from the Division of Research Grants and Fellowships of the National Institute of Health, U. S. Public Health Service.

Note by editor: Doctor Nelson was the recipient of the seventh annual award made by the American Urological Association for research on the male reproductive tract. Dr. Reed M. Nesbit, chairman of the Award Committee, read the following citation:

"Outstanding authorities have been chosen for this award, and each has brought to the annual meeting of the society a dissertation which has contributed to our knowledge of the reproductive process. This year, Dr. Warren O. Nelson has been chosen to be the recipient of the award. Doctor Nelson, Professor of Anatomy in the University of Iowa, has long distinguished himself for his research on the morphology and physiology of the testis in all species. He was one of the first to study depression of spermatogenic function by endocrine methods. This led to the observation of resurgent spermatogenesis at the withdrawal of the depressing agent, the so-called rebound phenomenon."

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Klinefelter syndrome) and prepubertal failure of the testes. We have considered the differential diagnosis of these three defects in other places[1, 2] and intend to go no further here than to say that differentiation of hypogonadotrophic eunuchoidism from the other two can be made readily on the basis of either, or both, testicular biopsy or assay of the patients urine for gonadotrophic hormone. In hypogonadotrophic eunuchoidism the testes are infantile and the urinary levels of gonadotrophin are very low. This latter finding is, indeed, the clue to the primary nature of the defect and assures us that the testes are intrinsically normal, lacking only the essential stimulating effect of the gonadotrophic hormones, FSH and ICSH, for their normal maturation. The defect then is one residing in the anterior pituitary and the testis is involved only secondarily. From the standpoint of relative incidence we have observed that 62 per cent of the individuals in a series of 148 eunuchoids fell into this category.

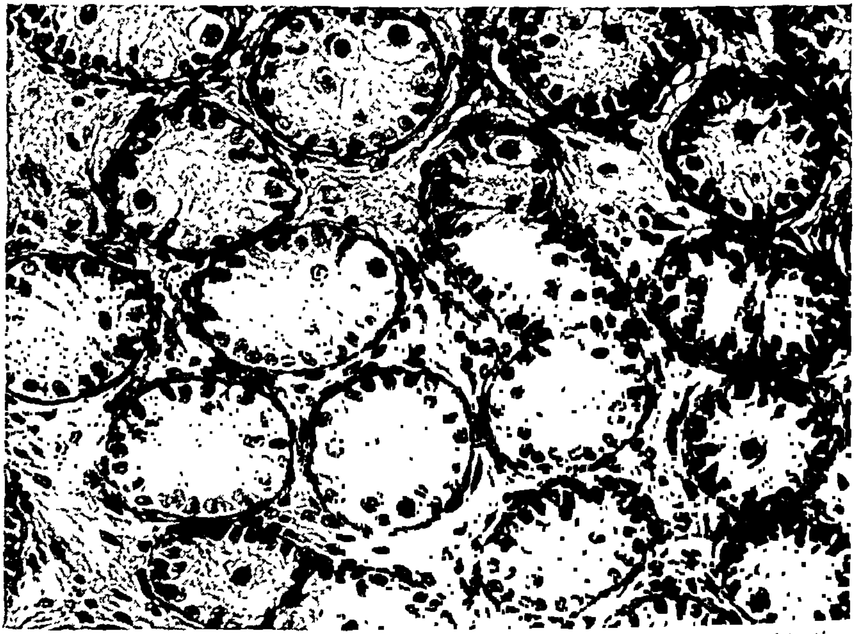

FIG. 1. Testicular biopsy from 23 year old eunuchoidal man. This is type of testis most commonly seen in hypogonadotrophic eunuchoids and is characterized by small tubules without lumens and containing undifferentiated Sertoli cells and spermatogonia with only rare primary spermatocytes. Leydig cells are absent. × 300

The characteristic picture observed in the testis is shown in figure 1. The tubules are very small, lack lumens and contain only spermatogonia and undifferentiated Sertoli cells, the intertubular areas contain numerous cellular elements, but none of these are differentiated Leydig cells. This histologic condition is identical with that of normal boys up to the onset of puberty and is so typical as to be unmistakable. However, although the large majority of testes in hypogonadotrophic eunuchoidism present this picture there are two variants which

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[1] Heller, C. G. and Nelson, W. O.: Classification of male hypogonadism and a discussion of the pathologic physiology and treatment. J. Clin. Endocrinol., 8: 345, 1948.

[2] Nelson, W. O.: Testicular morphology in eunuchoidal and infertile men. Fertility and Sterility, 1: 477, 1950.

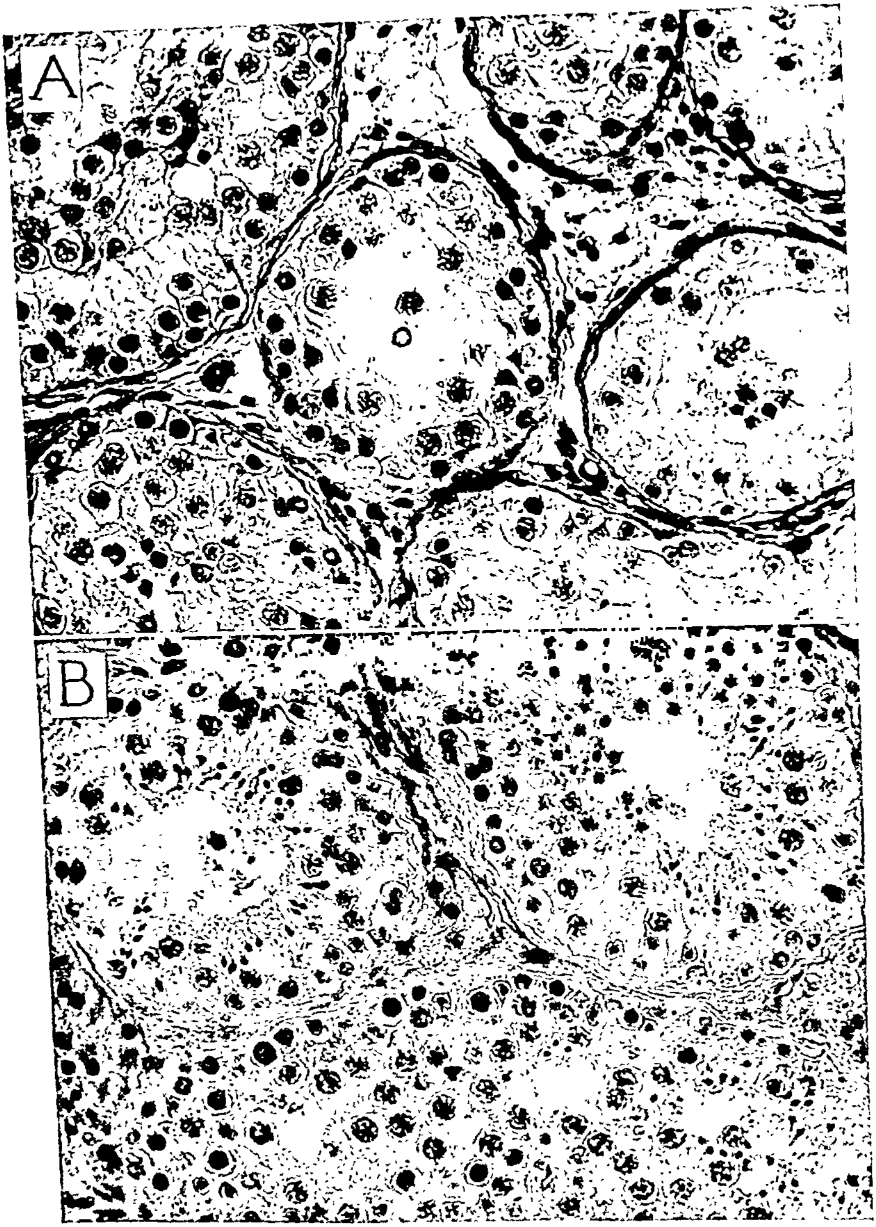

Fig. 2. *A*, testicular biopsy from 20 year old eunuchoidal man. Note that tubules are somewhat larger than in figure 1 and contain primary spermatocytes as well as spermatogonia. Leydig cells are absent. *B*, testicular biopsy from same patient after treatment with chorionic gonadotrophin. Note presence of spermatozoa and of Leydig cells. × 300

are encountered occasionally. In both of these the germinal cells are more numerous and the difference is distinct and consistent enough to suggest that the basic defects in the three conditions although similar are not identical.

In figure 2 it will be noted that significant numbers of primary spermatocytes are present in addition to the more primitive spermatogonia. In figure 3 cells of the entire spermatogenic series, including spermatozoa are found and although spermatogenesis is proceeding at a rate considerably below normal it is clear that formation of spermatozoa may occur in eunuchoidal men. However, further examination of figures 2 and 3 will show that they, as figure 1, lack Leydig cells and that the endocrine component of these testes appears not to have shared in the stimulus for maturation. This Leydig cell deficiency in the testes is reflected in the eunuchoidal status of their owners and suggests that the pituitary has secreted sufficient FSH to stimulate spermatogenesis, but has not provided the ICSH *essential for Leydig cell differentiation and function.*

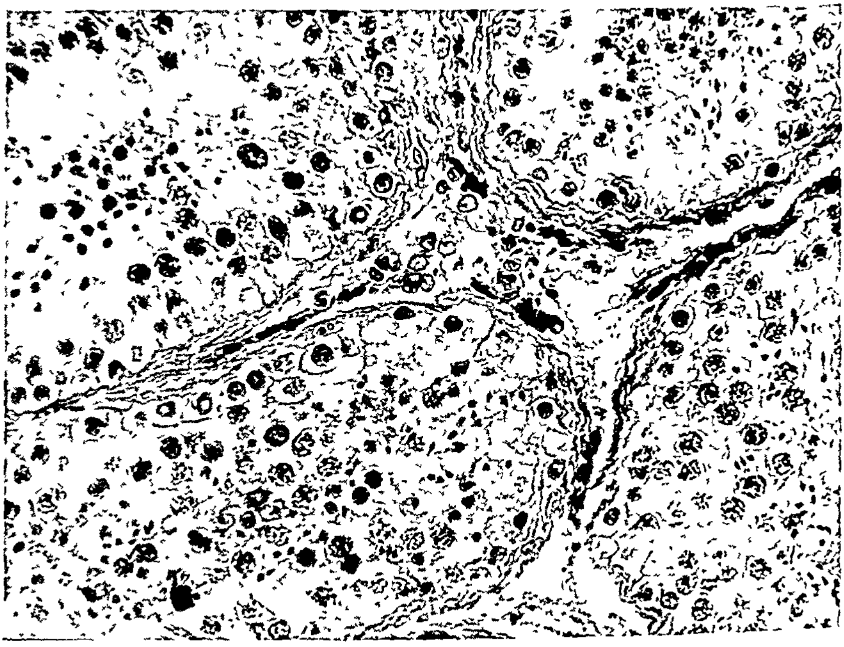

FIG 3 Testicular biopsy from 28 year old eunuchoidal man All stages of spermatogenesis including mature sperm are present, although total output of sperm is low Leydig cells are absent.

In 92 cases of hypogonadotrophic eunuchoidism in men at least 18 years old the distribution between the three categories which have been described was as follows:

1) Tubules with spermatogonia only or with spermatogonia and rare primary spermatocytes, 75.
2) Tubules with numerous primary spermatocytes, 8.
3) Tubules with all stages of spermatogenesis, 9.

It would be exceedingly interesting to be able to provide data for the levels of the two gonadotrophic hormones in these cases. Theoretically the larger group should show very low levels of both FSH and ICSH while the other groups should show increasing levels of FSH. Unfortunately most of the subjects in groups 2 and 3 from whom the biopsies were obtained were not available for sufficiently detailed urine collections and assays to permit such a study. Although in a few cases the assays suggested that small amounts of FSH, but not of ICSH, were present these data are incomplete and will require substantial additions before they will support the thesis that men in groups 2 and 3 produced more FSH than those in group 1. However, evidence which confirms this point has appeared in a recent brief report by McCullagh and Beck.[3] They found that the urines of 4 men who would be classified in group 3 showed the presence of FSH, but not of ICSH. McCullagh[4] in an earlier report on two eunuchoidal brothers was the first to call attention to the occurrence of spermatogenesis in the absence of Leydig cells. Indeed, material on these two cases, kindly supplied to me by Dr. McCullagh, represented the first two instances of the syndrome which I was privileged to observe.

It is noteworthy that the administration of ICSH, as represented by chorionic gonadotrophin, to men of group 2 has been followed by the formation of spermatozoa[5] and that the same treatment in men of group 3 has resulted in improved although still somewhat inferior spermatogenesis. Since Leydig cells, in both instances, were present in biopsies secured after treatment and since the production of androgen was manifest through the enhanced masculine status of the patients it is reasonable to suppose that the improvement in spermatogenesis was related to the addition of androgenic hormone. Although the evidence obtained in these cases cannot be regarded as complete the suggestion is clear that spermatogenesis in man can occur in conjunction with a deficiency of ICSH if FSH is present, but that normal spermatogenesis demands the presence of both gonadotrophic hormones.

THE FATE OF THE GERM CELLS IN THE UNDESCENDED TESTIS

For many years the question of the proper handling of cases of undescended testes has confronted us. Although there have been occasional protests the general consensus has been that no adverse changes occur in the undescended testis until after the advent of puberty. This has led to a tendency to temporize in treating the condition until age 12 to 15 years. In support of this practice the observation[6] that undescended testes occur in 10 per cent of newborn boys, and only 2.0 per cent and 0.2 per cent, respectively, of pubertal boys and adult men would indicate that of 100 cases of cryptorchidism at birth only 2 will be cryptorchid in adult life. Such statistics, as has been pointed out in another place,[7] indicate that only one man in 500 may be expected to be sterile as a result of undescended testes if, as has been generally assumed, no damage accrues to the undescended testis until puberty. However, if this assumption is erroneous approximately 10 per cent of human males are susceptible to injurious influences which may result in permanent testicular damage. That the undescended state of the testis actually may have deleterious effects upon the germ cells has been suggested by Felizet and Branca,[8] Burdick and Coley,[9] Cooper,[10] and Nelson.[7]

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[3] McCullagh, E. P. and Beck, J. C.: A syndrome of eunuchoidism with spermatogenesis and normal urinary FSH. Proc. Endocrine Society, p. 57, 1952.

[4] McCullagh, E. P.: Sex hormone deficiencies—some clinical considerations. Recent Progress in Hormone Research, **2:** 295, 1948.

[5] Nelson, W. O.: Interrelations of gonadotrophic and gonadal hormones in the regulation of testicular function. Ciba Foundation Colloquia on Endocrinology, IV. Anterior Pituitary Secretion. Philadelphia; Blakiston p. 271, 1952.

[6] Bishop, P. M. F.: Studies in clinical endocrinology. V. The management of the undescended testicle. Guy's Hospital Reports, **94:** 12, 1945.

[7] Nelson, W. O.: Mammalian spermatogenesis. Effect of experimental cryptorchidism in the rat and non-descent of the testis in man. Recent Progress in Hormone Research, **6:** 29, 1951.

These reports indicated that undescended testes tend to show fewer germ cells with continuation of the cryptorchid state and that differences between scrotal and undescended testes could be detected in prepubertal as well as postpubertal boys. Additional support for this thesis was provided by the observation[7] that as the state of surgically produced cryptorchidism in rats is prolonged fewer and fewer tubules are able to show spermatogenic activity when the testes are returned to the scrotum.

Although the evidence strongly suggests that the prepubertal undescended testis is subject to influences which reduce its spermatogenic capacity it can by no means be regarded as conclusive. The poor quality of spermatogenesis, which is so characteristic of the testis whose delayed descent has finally been effected by artificial means, may be due to constitutional defects of such gonads and therefore be another expression of the defective development which was responsible for the failure of descent. If this is true, at least in some instances of ectopic testes, the prognosis for fertility in such cases is dismal and may not be improved by treatment at any age.

Since consideration of this subject two years ago, additional material from boys and men with undescended testes has been studied. This material suggests that some cases of undescended testes are, indeed, associated with intrinsically defective populations of germ cells while in other instances the continuance of the ectopic state appears to have been responsible for a decrease in the number of spermatogenic elements.

In each of three boys, ages 6, 10 and 12 years, with unilateral cryptorchidism biopsies were obtained from the undescended testis as well as from the scrotal testis at the time of orchiopexy. In each instance the biopsies from both testes lacked germinal cells completely (fig. 4). This condition, designated as germinal cell aplasia, has been observed many times in the scrotal testes of adult men with azoospermia and is regarded, in some cases at least, as being due to the congenital absence of germinal cells. In one boy, age 10 with bilateral cryptorchidism biopsy of both testes at orchiopexy showed the same complete lack of germinal elements.

These observations indicate that some instances of testicular ectopia have a component of constitutional defectiveness and suggest that the paucity or lack of germinal cells in such cases is not due directly to the undescended state of the gonad, but rather to defects of development. Such defects occur in testes which do descend as well as in undescended testes.

Material has been obtained at biopsy or castration from six boys, ages 8 to 12 years, with unilateral cryptorchidism. In each case a biopsy of the scrotal testis

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[8] Felizet, G. and Branca, A.: Recherches sur le testicule en Ectopie. J. de la Anat. et de la Physiol., 38: 329, 1902.

[9] Burdick, C. G. and Coley, B. L.: Abnormal descent of the testicle. Ann. Surg., 84: 867, 1926.

[10] Cooper, E. R. A.: The histology of the retained testis in the human subject at different ages, and its comparison with the scrotal testis. J. Anat., 64: 5, 1929.

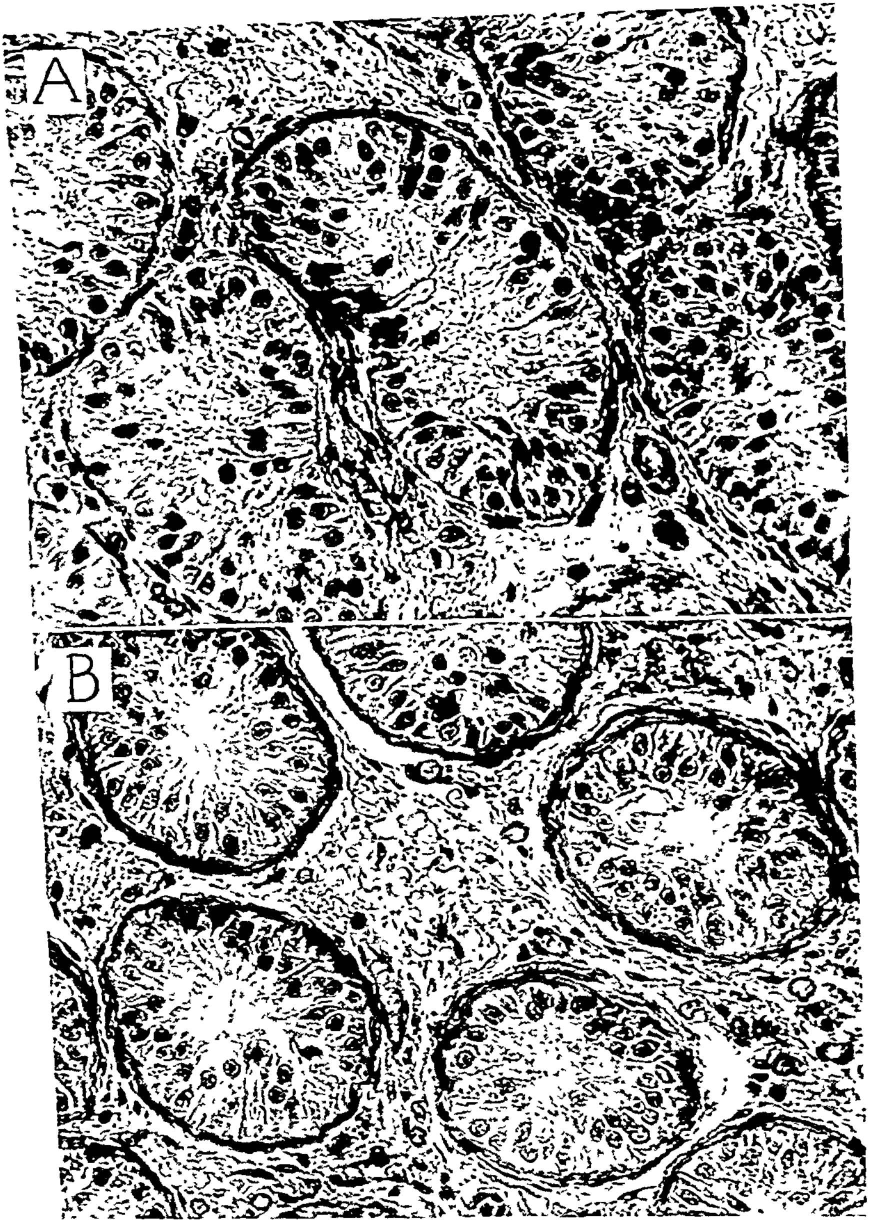

FIG. 4. *A*, biopsy from right scrotal testis of 12 year old boy. Germ cells are completely lacking Sertoli cells are undergoing differentiation. Leydig cells are typical of those seen in pubertal boys *B*, biopsy from left inguinal testis of same boy. Germ cells are absent and tubules are somewhat smaller than those in scrotal testis. Leydig cells are present. × 300

also was secured. The undescended testis in four of the six cases (ages 9, 10, 10, and 12 years) showed distinctly fewer germinal cells than did the scrotal testis from the same boy (fig. 5). In the remaining two boys (ages 8 and 9 years) both testes showed fewer than the expected number of germinal cells.

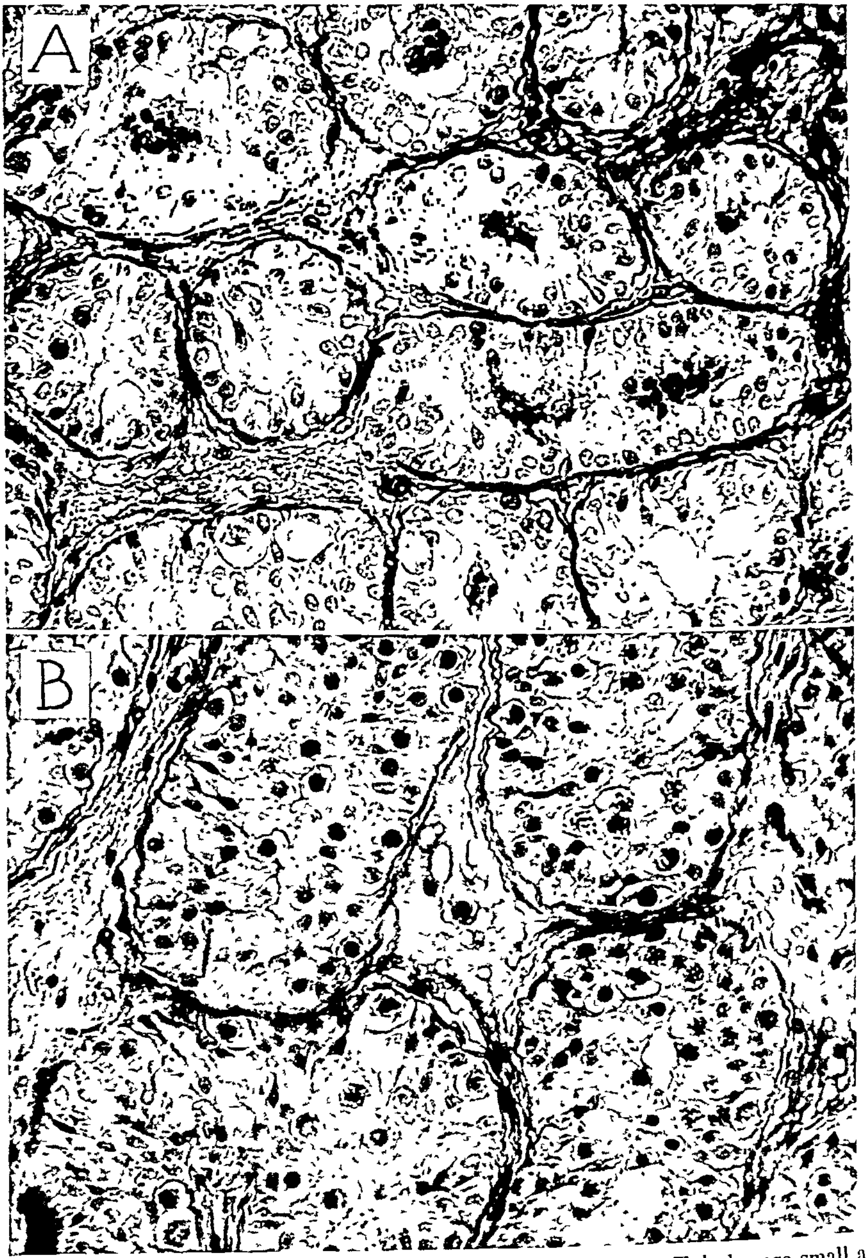

FIG 5. *A*, biopsy from right inguinal testis of 12 year old boy. Tubules are small and germ cells are relatively rare. Those present are spermatogonia Leydig cells are typical of pubertal boy. *B*, biopsy from left scrotal testis of same boy. Note that tubules are larger and that many spermatogonia and fairly numerous primary spermatocytes are present. Leydig cells are similar to those in inguinal testis × 300

In three men each complaining of infertility, histories of bilateral orchiopexy at ages 8, 12 and 14 years, respectively, were elicited. The total sperm counts averaged 35 million, zero and 8 million, respectively. The biopsy picture in the first instance showed fair spermatogenic activity in the majority of tubules, but rather severe peritubular fibrosis. In the second case germinal cells were completely lacking and in the third case less than 50 per cent of the tubules were carrying on a distinctly hypoplastic spermatogenesis.

Two men whose complaint was infertility gave a history of unilateral orchiopexy at age 12 years. Their total sperm counts averaged 15 million and 27.5 million respectively. In each instance biopsies were obtained from both the normally scrotal and the operated testes and in each instance the operated testes showed complete lack of sperm formation. The testes which had descended normally contained numerous tubules with severe fibrosis and hypoplastic spermatogenesis.

These data considered together with those reported earlier[7] indicate that the factors involved in cryptorchidism are multiple and that the response of the undescended testis to treatment will depend to a considerable degree upon the circumstances and factors which are present in a given case. Thus it is reasonable to suppose that in some cases the testes are constitutionally defective and that this defect may involve not only faulty development leading to an ectopic position, but also result in a paucity or complete absence of germinal cells. In other cases the gonads probably are intrinsically normal but fail to descend either because of inadequate hormonal stimulation or because of mechanical defects of the canal or associated structures. These testes are more likely to show spermatogenic activity, if descent is effected successfully before irreversible damage occurs, than testes which are constitutionally defective.

There is a very real need for long range studies on boys whose testes have had delayed descents. These studies should include instances of spontaneous descent as well as cases in which descent has been effected by surgical or homonal procedures. Close attention in these cases must be given to the factors—gonadal defectiveness, hormonal deficiencies or mechanical defects, which are responsible for testicular ectopia. When sufficient data on the condition of the testes and on the fertility performances of such men during their reproductive years are available we shall be in a much better position to evaluate the effect of the cryptorchid state upon the germinal cells and the response which treatment may be expected to invoke in individual cases.

GERMINAL CELL ARREST

The condition of complete germinal cell or spermatogenic arrest is encountered fairly frequently in men whose seminal specimens show lack of spermatozoa. In a series of 196 azoospermic, but otherwise normal, men it was observed 43 times, an incidence of 22 per cent. A similar condition, partial germinal cell arrest, has been encountered with approximately the same frequency in men whose seminal specimens averaged less than 60 million per cubic centimeter. In these cases of oligospermia a significant degree of arrest is seen only rarely in men whose counts are above 15 million per cc.

This defect of spermatogenesis is one in which the process of sperm maturation is halted at one of the immature stages, either completely or involving only part

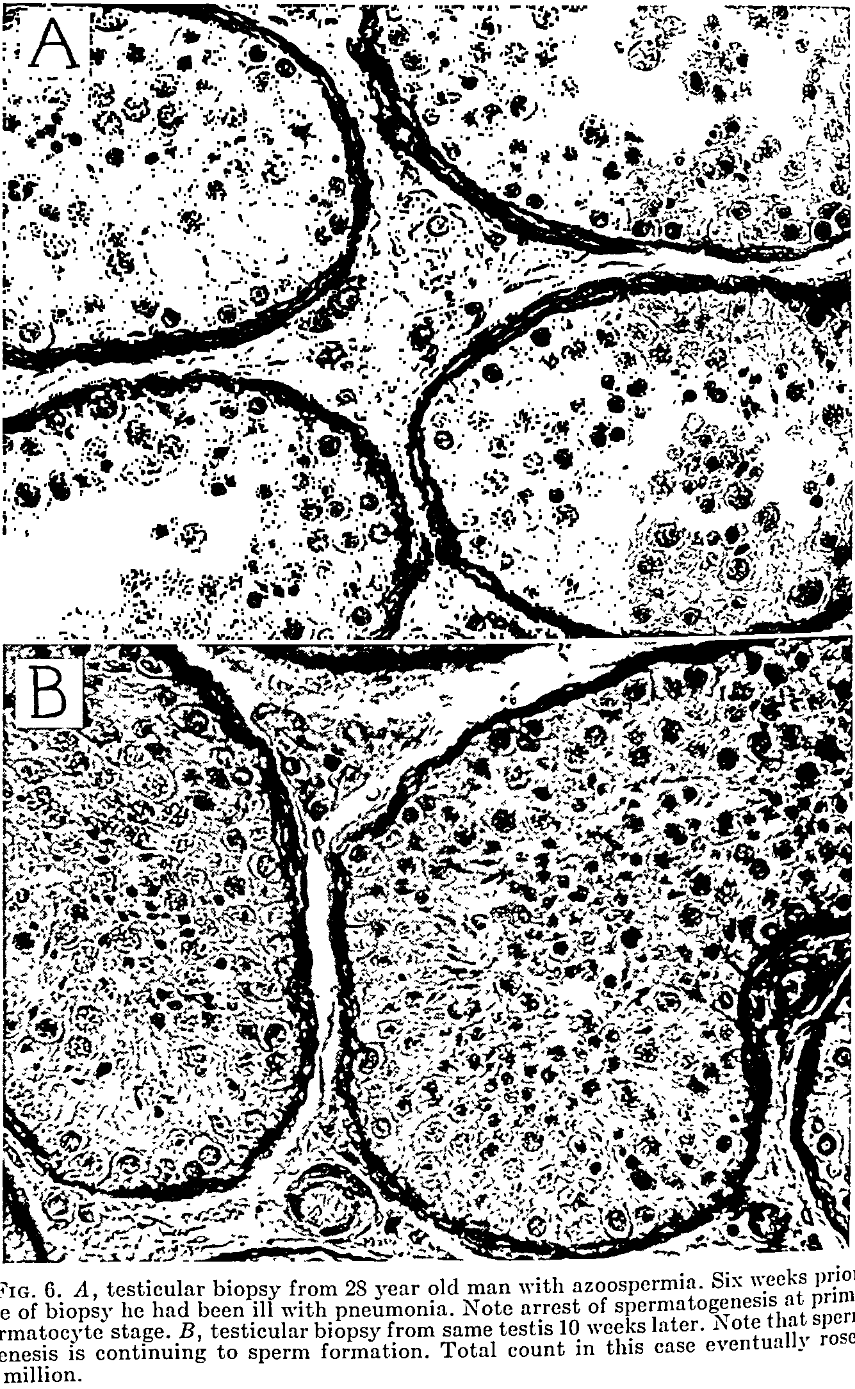

FIG. 6. *A*, testicular biopsy from 28 year old man with azoospermia. Six weeks prior to time of biopsy he had been ill with pneumonia. Note arrest of spermatogenesis at primary spermatocyte stage. *B*, testicular biopsy from same testis 10 weeks later. Note that spermatogenesis is continuing to sperm formation. Total count in this case eventually rose to 290 million.

of the cell population. In the vast majority of instances the stage at which arrest occurs is the primary spermatocyte and the testis presents a curious picture of tubules with spermatogenesis in progress but failing to proceed beyond that particular phase of the maturation process. One receives the impression that the primary spermatocyte is unable to complete successfully the complicated reduction division which normally results in the formation of secondary spermatocytes. Instead the nuclei either fragment or become pycnotic or engage in a bizarre type of division which ends in the formation of polynucleated cells. The result, of course, in the case of complete arrest is a total failure of production of spermatozoa. Where arrest is incomplete a relatively small number of cells appear to be able to complete the reduction division and to continue the spermatogenic process.

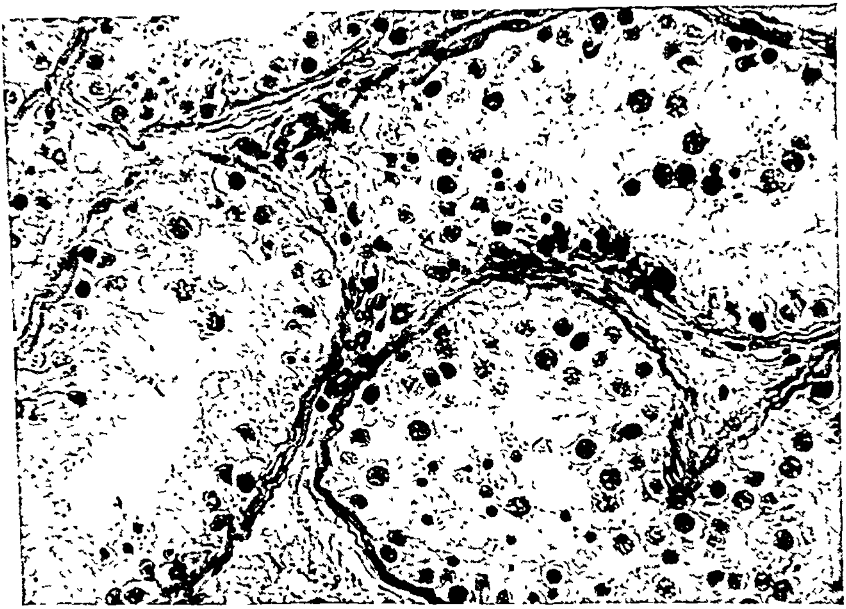

FIG. 7. Testicular biopsy from 26 year old man who gave a history of radiation of pituitary for chromophobic adenoma at age 16. Spermatogenesis is arrested at primary spermatocyte stage. × 300

In the much less frequently observed conditions of arrest at the spermatogonium and secondary spermatocyte stages the end result, of course, is a similar one, i.e., total failure of sperm production if the process affects all cells or a much reduced output of spermatozoa in the case of incomplete arrest.

The etiologic factors which are related to or involved in germinal cell arrest are incompletely understood, but it is of interest to note the variety of conditions in which we have observed the defect and the factors which appear to contribute to it.

1) Diseases in which the body temperature is significantly elevated. These have included pneumonia, measles, chicken pox and undulant fever (fig. 6).
2) Insulating effects of tight fitting jockey type shorts.
3) Occupations in which the individual is subjected to very high temperatures for many hours.
4) Some instances of undescended testes.

5) Some instances of deficiency of gonadotrophic hormones. These have included eunuchoidism (fig. 2), tumors of the pituitary, and conditions arising after hypophysectomy (complete in the rat; probably incomplete in man) or x-irradiation of the hypophysis (fig. 7).
6) Following the administration of certain drugs, e.g., nitrofurans (fig. 8).

In this list it will be noted immediately that the first four conditions have the common denominator of elevated temperature. For many years the deleterious effect of elevated temperature upon spermatogenesis has been recognized and many experiments have shown that the cooler environment normally provided by the scrotum, in animals which possess that structure, is essential for complete spermatogenesis. However, under some circumstances the scrotum is unable to maintain the necessary temperature difference and spermatogenesis is halted at the primary spermatocyte stage. The disturbed spermatogenesis in these cases need not be permanent, particularly if the conditions contributing to it are corrected before peritubular fibrosis intervenes.[11] Indeed, serial biopsies of the testes of men whose arrested spermatogenesis was attributed to diseases such as pneumonia, to occupational heat, or to the insulating effects of tight underwear have shown that correction of these conditions results in the resumption of complete spermatogenesis. It has been possible, furthermore, to follow the return of spermatogenesis in these men by examination of serial seminal specimens. MacLeod's[12] and Brown's[13] observations on the seminal fluids of men recovering from pneumonia, chicken pox and stomatitis have been particularly interesting.

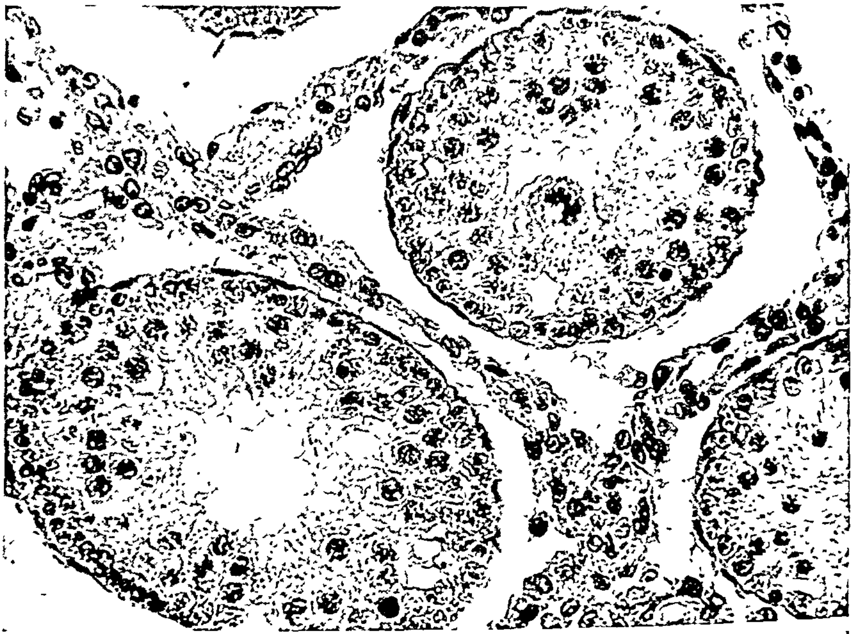

FIG. 8. Testis from a rat which had received treatment with nitrofuran compound for 30 days. Spermatogenesis is halted at primary spermatocyte stage. × 300

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[11] MacLeod, J. and Hotchkiss, R. S.: The effect of hyperpyrexia upon spermatozoa counts in men. Endocrinology, **28**: 780, 1941.

[12] MacLeod, J.: Certain concepts in human male infertility. J. Urol., **67**: 19, 1952.

The relation of the fifth condition listed above to arrested spermatogenesis is equally clear since it involves a lack of the gonadotrophic hormones essential for the spermatogenic process. In such cases it has been possible to stimulate spermatocyte divisions and the formation of spermatozoa by the administration of gonadotrophic hormones.

The sixth factor in the list, i.e., drugs, has not been shown to cause germinal cell arrest in the human testis, but interesting observations have been made in animals and it is by no means unlikely that a similar effect exists in man. Thus it has been shown that administration of the nitrofurans in rats causes arrest at the primary spermatocyte stage (fig. 8) with recovery when the drug is withdrawn.[14, 15] The experiments of Paul, Paul and Kopko[16] suggest that the causative factor in this case may be the effect of the drug upon the capacity of the testis to metabolize carbohydrate, presumably through deleterious influences upon essential enzymatic processes.

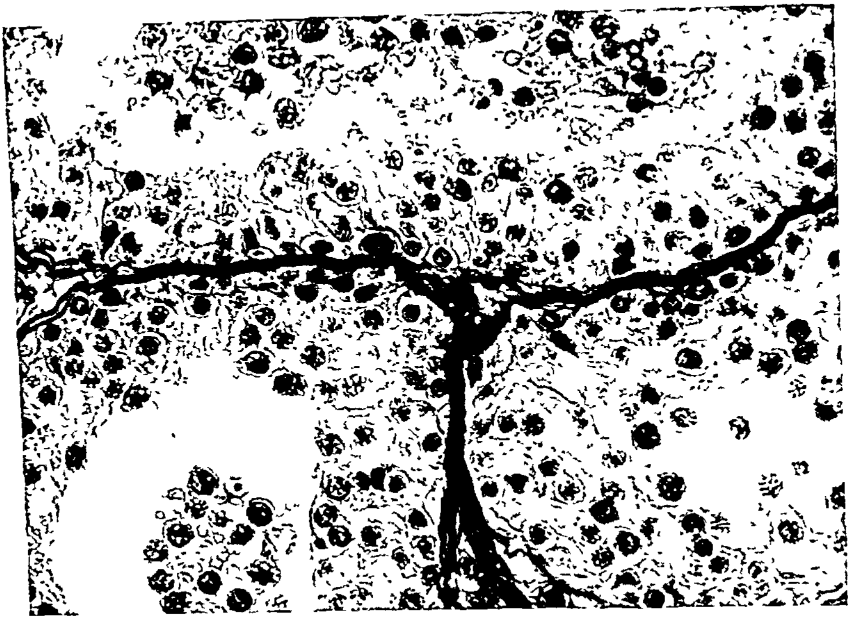

FIG 9 Testicular biopsy from 31 year old man whose seminal specimens showed azoospermia Although no etiologic factors responsible for condition could be detected, spermatogenesis shows picture of arrest. × 300

Thus we may list the following factors as being of probable significance in the production of germinal cell arrest:

1) Elevated temperature.

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[13] Brown, R L Sperma transport in man J. Urol , 50: 786, 1943

[14] Prior, J T and Ferguson, J H. Cytotoxic effects of a nitrofuran on the rat testis Cancer, 3: 1062, 1950

[15] Nelson, W O. and Steinberger, E. The effect of furadroxyl upon the testis of the rat Anat Rec , 112: 367, 1952

[16] Paul, H E , Paul, M F and Kopko, F.· Effect of furacin (5-nitro-2-furaldehyde semicarbazone) on the *in vitro* metabolism of mammalian tissues Proc. Soc. Exp Biol. and Med , 79: 555, 1952

2) Deficiency of gonadotrophic hormones.
3) Interference with enzymatic mechanisms.

Of course, it is quite possible that the last of these is the really significant factor and that elevated temperature and gonadotrophin deficiency become important only through their effects upon enzymatic processes.

Although it has been possible in some instances to ascribe arrested spermatogenesis to one or another of the conditions which have been listed, in the majority of cases even the most painstaking attempts to obtain enlightening evidence from the physical and medical examinations and from the histories have failed (fig. 9). In these men one is forced to assume the existence of some undetected factor, the presence of residual effects which originated in some early disease or experience, or that the germinal cells are constitutionally defective. The fact that arrested spermatogenesis in this group of men can only rarely be corrected suggests strongly that the latter alternative may be a significant factor in many cases of germinal cell arrest. Conceivably the defect may reside in the chromosomes and become evident when they attempt to undertake the complex synaptic changes which occur during the reduction division.[2, 17] If such is true it is unlikely that attempts to improve spermatogenesis will be successful until the basic nature of the chromosomal defect is ascertained. In these cases, too, it is possible that important enzymatic mechanisms are at fault and that corrective measures will become available as our understanding of such processes advances.

In summarizing the observations on germinal cell arrest it may be said that this defect is not necessarily permanent when it occurs as a result of certain extrinsic or intrinsic factors which are inimical to spermatogenesis if those factors are eliminated or corrected, but that it is probably not susceptible to correction at the present time in cases where chromosomal aberrations appear to be present.

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[17] Engle, E. T.: Questions on the cytodynamics of spermatogenic arrest of the human testis. Ann. New York Acad. Sciences, **55**: 703, 1952.

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ANATOMIC ALTERATIONS OF THE ADRENAL CORTEX

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Tumors of the adrenal cortex are of great interest because of the striking clinical conditions with which they are often associated. These include masculinization of women, feminization of men, precocious sex development of children, and Cushing's syndrome. Such interesting conditions are the clinical expressions of tumors that elaborate ketosteroids with androgenic or estrogenic effects. These remarkable changes have eclipsed the interest in non-functioning lesions of the adrenal cortex. The purpose of this paper is to comment on the anatomic alterations of the adrenal cortex that are not associated with hormonal disturbances and that are not malignant. The description of an unusual lesion of this type is included in the case report of a large benign cortical adenoma. Emphasis is directed to the clinical similarities of those cases from the literature in which large cortical adenomas are described.

It is not always possible to distinguish hyperplasia from neoplasm or from misplacement of adrenal cortical cells. However, common and benign anatomic alterations of the adrenal cortex occur in three separate forms. These include the extracapsular free cell cluster, the adrenal cortical nodule, and the adrenal cortical adenoma. Each is to be described separately.

Extracapsular free cell clusters are minute collections of cortical cells that lie loose in the fibro-adipose tissue immediately outside of the adrenal capsule (fig. 1, *A*). These cortical cell clusters are described under the term anatomic alterations because they are not known to be of clinical importance and because they are extremely common. Examination of one microscopic section taken at random from each of 200 otherwise normal adult adrenals revealed 17 extracapsular cortical cell clusters. It appears likely that serial sections would demonstrate these clusters about most adrenals. They are usually present about both adrenals and are often widely separated from the peri-adrenal region, being particularly common over the surface of the kidneys. Weller[1] stated that portions of adrenals, usually composed of cortex only, may be found in practically every cadaver in which careful search for them is made. However, he emphasized that this does not represent true heterotopia which he takes to mean displacement of the entire adrenal.

The second anatomic irregularity is the adrenal cortical nodule. This structure is composed of a round, compact collection of adrenal cortical cells lying just outside the adrenal capsule encased within a thin layer of fibrous connective tissue (fig. 1, *B*). The adrenal cortical nodule is ordinarily not considered to be a lesion because of its frequency and because it is not known to be associated with a clinical disturbance. Microscopic examination of a single section taken

Accepted for publication April 30, 1952.

[1] Weller, C. V.: Heterotopia of the adrenal in liver and kidney. Am. J. Med. Sci., **169:** 696, 1925.

at random from each of 200 otherwise normal adult adrenals disclosed 31 adrenal cortical nodules. These nodules are usually present about both adrenals and it is likely that serial sections would demonstrate a much higher incidence. Adrenal cortical nodules are then minute, bilateral, extracortical, and of no known clinical importance.

The third form of anatomic alteration of the adrenal is the cortical adenoma. This term is inaccurate because adrenal cortical cells are of mesodermal origin and the cells ordinarily do not form acini. However, the term has the sanction of established usage. The adrenal cortical adenoma differs from the free cell cluster and from the cortical nodule in several respects. The adenoma is present within the cortex and often measures 1 to 4 cm. in diameter (fig. 2). It is usually present on one side only, and may be associated with a clinically evident hormonal imbalance. It is to be emphasized that the lesion is not uncommon and that the great majority of adrenal cortical adenomas are not associated with endocrine disturbances. Examination of the last 500 consecutive autopsy records of Wesley Memorial Hospital revealed 21 adrenal cortical adenomas that exceeded 0.7 cm. in diameter. The largest measured 6 cm. in diameter. All were unilateral and none was associated with a clinically detectable disturbance of hormone production of androgenic or estrogenic type. That few adrenal cortical adenomas are associated with endocrine disturbances is also indicated by Russi and Blumenthal[2] who described 131 cases without such changes. In a series of 66 adrenal cortical adenomas or localized hyperplasias, Geschickter[3] found three

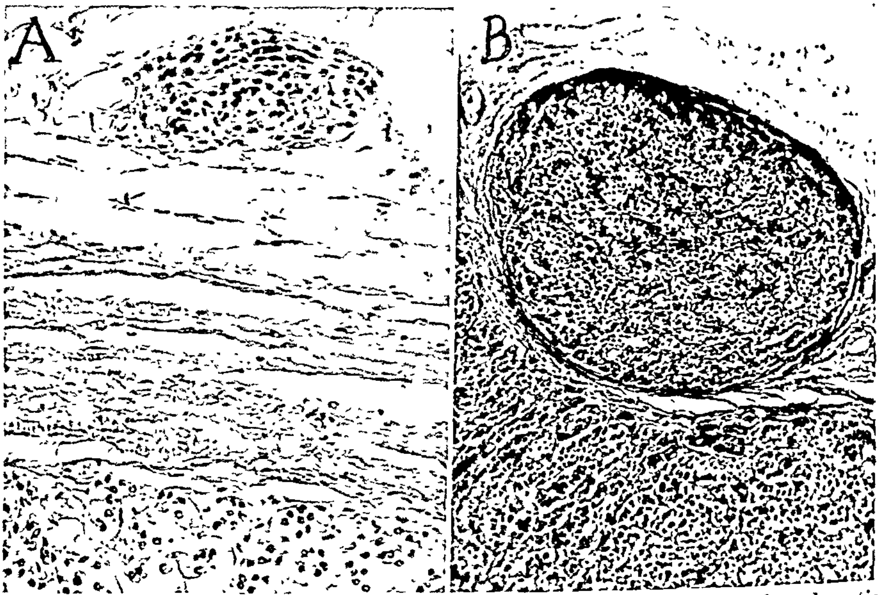

FIG. 1. *A*, extracapsular free cell cluster of adrenal cortical cells. *B*, adrenal cortical nodule.

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[2] Russi, D., and Blumenthal, H. T.: Small adenomas of the adrenal cortex in hypertension and diabetes. Arch. Int. Med., 76: 284, 1945.

[3] Geschickter, C. F.: Suprarenal tumors. Am. J. Cancer, 23: 104, 1935.

that were clinically evident and in only one of these, a precocious male child, was the endocrine nature of the disturbance established. Adrenal cortical adenomas are then common, macroscopic, unilateral, intracortical, and are not often associated with endocrine disturbances. A comprehensive review of adenomas of the adrenal cortex is reported by Kepler and Keating.[4]

Occasionally the nonfunctioning adrenal cortical adenoma attains large size. When this occurs, a combination of signs and symptoms develops that probably represents a clinical entity. Only 4 cases of such adenomas of the adrenal cortex have been found in the English literature. Because of the clinical similarities of these cases, and the paucity of reports recording their descriptions, the present case is of interest.

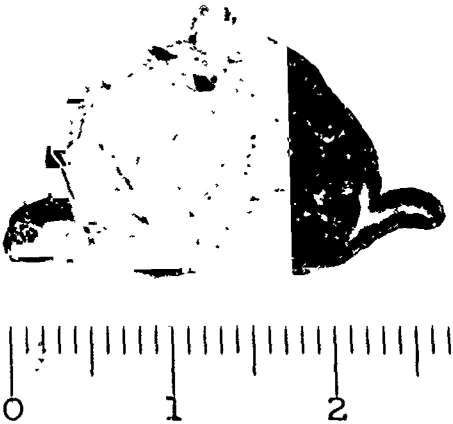

FIG. 2. Cut surface of adrenal cortical adenoma with centimeter scale

CASE REPORT

A white woman 47 years old was well until 2 years before entering the hospital. At that time she noted a sensation of fullness in the left upper quadrant of the abdomen and shortly after this there was a gradual increase in waist size. These changes were slowly progressive so that difficulty in the fitting of clothes developed. There were no other comlpaints until one month before hospital admission when a sharp and constant pain developed in the left lower abdomen that radiated to the left upper quadrant. The pain was of 2 days duration and subsided after an enema. The fecal return appeared normal and at this time the patient first noted a vaginal discharge that contained bright red blood and clots. Slight vaginal bleeding persisted. There had been no constipation although there was a sensation of incomplete defecation during the 3 weeks before admission. There had been no nausea, vomiting, anorexia, loss of weight, melena or other symptoms referable to the genito-urinary tract.

A supracervical hysterectomy had been performed 7 years before the present

[4] Kepler, E. J., and Keating, F. R.: Diseases of the adrenal glands. II. Tumors of the adrenal cortex, diseases of the adrenal medulla and allied disturbances. Arch. Int. Med., 68: 1010, 1941.

illness because of excessive menstrual bleeding. Moderate hypertension had been present for the past 4 years and exertion was occasionally accompanied by weakness and palpitation. Hyperthyroidism had been present for the past 3 years and the patient was taking 10 drops of Lugol's solution and 1½ gr. phenobarbital three times daily at the time of admission.

Physical examination revealed a small under-developed and poorly nourished white female who did not appear acutely ill. The temperature was 99 F, pulse 92, respirations 22, and blood pressure 168/96 mm. Hg. There was no exophthalmos and the head was normal. The thyroid was firm, smooth, symmetrical and barely palpable. The chest was clear to percussion and auscultation of the heart and lungs were normal. The abdomen was moderately distended and non-tender. A firm mass was present in the left abdomen that extended from the costal margin to the left iliac crest. The inferior border of this mass was smooth, firm and tender. The upper border of the mass was separate from the spleen. The mass did not move with respirations. The liver margin extended to the right iliac chest. Rectal and pelvic examinations revealed only absence of the body of the uterus, and a small cervical erosion. The extremities were normal. There was no enlargement of peripheral lymph nodes and neurologic examination was normal.

Urinalysis was normal except for a trace of protein. Hematological examination revealed 14 gm. of hemoglobin per 100 cc. There were 4,600,000 erythrocytes and 10,700 leukocytes per cu. mm. Differential count of 100 cells disclosed 68 segmented granulocytes, 6 band cells, 23 lymphocytes, 2 eosinophils and 1 monocyte. The platelet count was 372,000 per cu. mm. and the prothrombin time was 98 per cent. The sternal marrow was normal. After an intramuscular injection of adrenalin there was no change in the blood leukocyte count or in the size of the abdominal mass. Total plasma protein was 5.8 gm. per 100 cc with 3.0 gm. of albumin and 2.8 gm. of globulin. Thymol turbidity was less than 1 unit. X-ray examination of the chest revealed only slight increase in the transverse diameter of the heart. X-rays of the abdomen disclosed a large mass on the left side, containing small foci of calcification that displaced the stomach medially and the splenic flexure of the colon and the left kidney downward. In addition, the liver margin extended to the right iliac crest.

On the eleventh hospital day the abdomen was entered through a left pararectus incision that was enlarged by an extension into the flank. A large retroperitoneal encapsulated mass on the left side was encountered that displaced the left kidney and transverse colon downward. In addition, that part of the liver lying on the left side of the midline was displaced downward and to the right. The tumor was excised, and in so doing, excessive bleeding was encountered about the splenic pedicle so that a splenectomy was performed. In addition, the gallbladder was removed. The abdomen was then closed and the patient recovered uneventfully.

Examination of the pathologic specimen (WMH-S-61309) revealed a somewhat lobulated, firm, encapsulated, yellow, mottled with red tumor that weighed 1578 grams. The surface was roughened by fibrous tags and the cut surface was pink mottled with broad zones of gray, yellow and dark red (fig. 3). Microscopic examination revealed vast sheets of uniformly large cells with small round basophilic nuclei and abundant clear pale pink cytoplasm (fig. 4). At separate sites there were extensive recent hemorrhage, wide zones of necrosis, and scattered clusters of fat cells. The anatomic diagnosis was cortical adenoma of the adrenal. Examination of the gallbladder disclosed slight chronic cholecystitis with cholelithiasis. The spleen weighed 174 gm. and was not unusual.

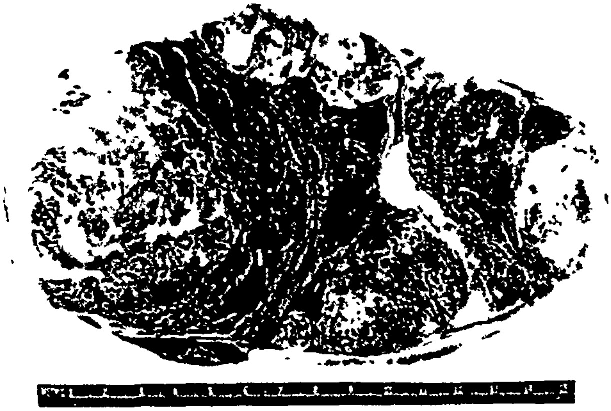

FIG. 3. Cut surface of large adrenal cortical adenoma

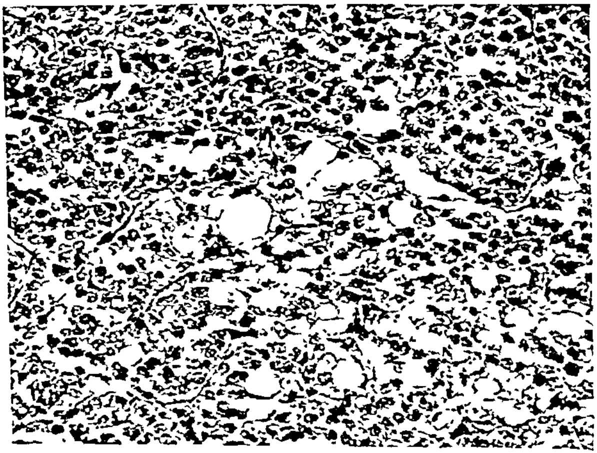

FIG. 4. Microscopic appearance of large adrenal cortical adenoma

COMMENT

Clinically it was difficult to associate the apparent enlargement of the liver with a slowly enlarging mass on the left side of the abdomen and the vaginal bleeding. After operation, it was apparent that the hepatic factor was one of displacement rather than enlargement. It is assumed that the vaginal bleeding was related to the pronounced venous stasis in the pelvis. However, bleeding from the cervical erosion is not excluded. Anatomically it is to be emphasized, according to Karsner,[5] that microscopic examination of adrenal carcinomas usually reveal no pleomorphism of cells, abnormalities of mitotic figures, or other features common to malignant tumors that would lead to a positive diagnosis. However, in this case there were no clinical signs of metastasis, none was demonstrated at the time of operation, and the patient has been well for a period of 8 months after the operation.

DISCUSSION

Similar cases of large nonfunctioning adenomas of the adrenal cortex have been reported by Loeb,[6] Timoney[7] and by Lumb.[8] These are summarized in table 1. Although the number of cases is small, the recurrence of certain unique features suggests that a clinical entity is produced.

The unique clinical features of this condition include the occurrence of a slowly enlarging tumor of the upper abdomen, not attached to the kidney, that displaces the colon and kidney downward. Compression and displacement of the colon and kidney are manifest by signs referable to the gastro-intestinal and genito-urinary systems. These include for the former, anorexia, constipation, and colicky pain, and for the latter, dysuria and urgency. Although proof is lacking that the reported tumors were benign because the postoperative period of observation was short in each case, there were also no indications of malignancy either by clinical evidence of metastasis, microscopic examination of the tumor, or by gross examination of the abdominal organs at the time of operation. Nevertheless, weakness and malaise were prominent. In the case of Loeb, a 40 pound loss of body weight occurred during a 2 year period and the report of Timoney describes an obese female with a loss of 107 pounds of body weight during a similar period. The latter patient was at one time deemed inoperable because of a clinical diagnosis of malignant tumor. Endocrine disturbances of estrogenic or androgenic nature were not present. One patient of Timoney was obese, and pronounced hypertension was present in the first case described by Lumb. However, in this case there was prostatic enlargement and after death autopsy examination was not performed and the state of the kidneys was not described. All patients survived operative removal of the tumor and recovery was uneventful except in the two cases of Lumb in which death occurred on the sixth post-operative day. In both cases this was ascribed to pneumonia and in neither case was an autopsy performed. It is of interest that a case of adrenal cortical adenoma with absence of the opposite adrenal has been reported.[9]

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[5] Karsner, H. T.: General pathology of tumors of endocrine glands. Bullet. N. Y. Acad. Med., **22:** 503, 1946.

[6] Loeb, M. J.: A case of adrenal cortical tumor without endocrinological symptoms. J. Urol., **45:** 785, 1941.

[7] Timoney, F. X.: Nonhormonal adrenal adenoma: Case report. J. Urol., **49:** 654, 1943.

[8] Lumb, G. Adrenal cortical tumors of unusually large size. Brit. Med. J., **1:** 582, 1950.

[9] Lukens, F. D. W., Filippin, H. F. and Thigpin, F. M.: Adrenal cortical adenoma with absence of opposite adrenal; report of case with operation and autopsy. Am. J. Med. Sci., **193:** 812, 1937.

Death followed removal of the tumor. In addition, Weinberg[10] pointed out that in cases of cortical adrenal tumor, atrophy of the opposite adrenal may occur. Cahill[11] suggests identification of the normal adrenal by perirenal air insufflation on the side opposite the tumor before operation.

The clinical features of large nonfunctioning adrenal adenomas were recognized by Langeron and Loheac[12] who emphasized the slow progressive enlargement of an upper abdominal tumor associated with pain in the lumbar region and vague digestive disturbances. However, other conditions may be clinically similar and these include carcinoma of the adrenal cortex, carcinoma of kidney, tumor or nontumorous enlargement of the spleen, pseudocyst of the tail of the pancreas, and retroperitoneal sarcoma. Carcinomas of the adrenal cortex often

TABLE 1. *Large non-functioning adrenal cortical adenomas*

AUTHOR	AGE	SEX	TUMOR	DURATION	SIGNS AND SYMPTOMS
Loeb	48	F	1100 Gms.	2 years	Slowly enlarging upper abdominal tumor associated with pain Weakness, malaise, 40 pound weight loss. Downward displacement of colon and kidney
Timoney	37	F	4200 Gms.	2 years	Slowly enlarging upper abdominal tumor associated with "dragging" sensation Anorexia, constipation and urgency. 107 pound weight loss Downward displacement of kidney Medial displacement of colon
Lumb (Case 1)	69	M	3750 Gms.	5 mos.	Upper abdominal tumor associated with dysuria Pyelograms normal X-rays of colon not reported
Lumb (Case 2)	57	F	5350 Gms.	3½ years	Slowly enlarging upper abdominal tumor associated with colicky pain and mild constipation Pyelograms normal Downward displacement of colon

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[10] Weinberg, T.: Contralateral adrenal atrophy associated with cortical adrenal neoplasms. N. Y. State Med. J., 41: 884, 1941.

[11] Cahill, G. F.: Air injections to demonstrate adrenals by x-ray. J. Urol., 34: 238, 1935.

[12] Langeron, L., and Loheac, P.: Formes cliniques des tumeurs malignes primitives des capsules surrenales. Ann. De Medecine, 23: 17, 1928.

attain large size as 33 of 82 cases collected by Wu[13] were palpable. The weight of these tumors was listed in 23, and in 18 that weight exceeded 1,000 gm. In 63 of these 82 adrenal carcinomas there were distinct endocrine disturbances of androgenic or estrogenic nature. This feature, together with evidence of metastatic growth, ordinarily serves to distinguish the adrenal carcinoma from the non-functioning adenoma. Displacement of the colon is minimal in carcinoma of the kidney and metastatic growth, frequently in the lungs, is usually present before the tumor attains large size. In a series of 149 carcinomas of the kidney reported by Bell,[14] metastases were present in 66 of 84 in which the tumor exceeded a diameter of 5 cm. Enlargement of the spleen is usually detectable by diagonal movement of the organ across the abdomen with respiration and thus differs from the fixed retroperitoneal tumors. Pseudocysts of the tail of the pancreas are usually solitary, often large, and may project outside of the organ to constitute a large abdominal mass. Onset after trauma, roentgen demonstration of the mass lying between the stomach and colon,[15] and identification of a normal adrenal by insufflation of air aid in excluding the diagnosis of large adenoma of the adrenal cortex. Retroperitoneal malignant tumors, of which liposarcoma is the most frequent, are often of slow growth, large size and late metastatic spread.[16] However, the liposarcoma is not ordinarily a sharply demarcated tumor in one portion of the abdomen and perirenal air insufflation may disclose a normal adrenal.

SUMMARY

Anatomic alterations of the adrenal cortex occur in three separate forms. These include extracapsular free cell clusters, adrenal cortical nodules, and adenomas of the adrenal cortex. The first two are minute, common, usually bilateral, extracortical, of no known clinical importance, and differ in that the latter are encased in a narrow rim of fibrous connective tissue. Adenomas of the adrenal cortex are usually macroscopic, intracortical, unilateral, and uncommonly associated with endocrine disturbances. Large nonfunctioning adenomas of the adrenal cortex are characterized by slow enlargement of a palpable upper abdominal tumor associated with symptoms referable to the gastro-intestinal and genito-urinary systems and without evidence of metastasis or endocrine disturbance. Weakness, malaise and loss of weight may be prominent. Roentgen examination discloses downward displacement of the colon and kidney on the side of the tumor. Excision is curative. An additional case of large nonfunctioning adenoma of the adrenal cortex is described.

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STAGHORN CALCULI

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The management of the patient with staghorn renal calculi is usually an intriguing clinical experience. One frequently begins by marvelling at how these stones may achieve such impressive size and bring about such extensive destruction of the renal substance without giving rise to more in the way of subjective symptoms. It is not uncommon to find that the patient has actually had no discomforts at all, and that the diagnosis is made only in tracking down the cause of pyuria discovered in a routine physical examination, an insurance examination, or perhaps because the stone shadows were seen in x-ray studies made for some unrelated purpose. In a small percentage of cases, a careful history will elicit a story of what may have been previous episodes of renal colic due to the passage of lesser calculi. Had these episodes been adequately investigated, the fundamental problem might have been uncovered at an earlier date.

The problems presented by staghorn calculi (renal) are diversified. The urologist is obliged to consider possible etiological factors, to assess the advisability of surgical removal, to evaluate medical measures for control, and to cope with the ever-present threat of recurrence. The patient who has once had staghorn calculi is an individual who requires urological supervision for life, and the length of that life may be peculiarly dependent upon the judgment of the physician.

ETIOLOGY

Much that concerns the development of urinary calculi is still controversial or obscure, and it is not our purpose here to review the conflicting evidence Certain factors are of importance beyond a reasonable doubt First, there is the matter of heredity. We regard the tendency to form primary urinary tract calculi as a family characteristic in certain instances. Inasmuch as this factor is not one of much value in the management of any given case, we will not dwell on it except to remark that recently, after removing a staghorn calculus from the right kidney of a young man and learning that we had previously removed calculi from his father and that a brother was currently in an Army hospital for the removal of stones from both kidneys, we suggested that his remaining brother stop by for a check-up. He also showed asymptomatic renal calculi.

Metabolic abnormalities are also of significance. Cystinuria is of importance, although our incidence of cystine stones has been extremely low. It follows, however, that the discovery of cystinuria materially affects the prognosis for the formation of future stones, and the medical measures taken to minimize the possibility of such recurrence. Much the same may be said of urate and uric acid stones occurring in persons who show a high blood uric acid. More intriguing is the problem of hyperparathyroidism and the formation of calcium stones.

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Here it is an incontestable fact that the existence of a parathyroid adenoma may lead to hypercalcemia, hypercalcinuria, and the development of nephrocalcinosis or renal calculi. Whereas it has been our routine practice over the years to carry out blood calcium and phosphorus studies on all stone-forming patients, we must admit that we have felt only once that parathyroid exploration was desirable and in that instance no adenoma was found. Our lack of cases of hyperparathyroidism is not assignable to a negligence in looking for the condition. Since we are specifically discussing the so-called staghorn type of calculus, it seems necessary to admit that we have encountered a recognizable metabolic abnormality in only a handful of cases, and that when such abnormality has been recognized there has proved to be little modifiability of the situation.

Of more practical importance is the matter of stasis of urine. When an obstructive factor can be identified, it must be dealt with accordingly, since simple removal of the stone will be followed by recurrence in virtually every instance if the obstruction persists. It should be emphasized that one must not conclude that there is no stasis simply because the ureteropelvic junction is not obstructive in character. The lower end of the ureter is a frequent offender in unilateral cases, and the vesical neck and the external urethral meatus must be regarded with suspicion in bilateral cases. The effect of prolonged recumbency and immobilization is also to be considered under the heading of stasis, and its role is usually obvious.

Lastly, we must consider infection. At the present time, there are effective means of combating virtually every organism encountered in cases of calculous disease. The urea-splitting organisms are obviously of principal importance since, by their strong alkalinization of the urine, they favor the formation and rapid growth of stones. Among them have been some of the more troublesome organisms in terms of resistance to chemotherapeutic or antibiotic treatment. Now, under proper circumstances, it is possible to eradicate the urea-splitting staphylococci with a variety of medications. Bacillus proteus yields quite decently to gantrisin, and Bacillus pyocyaneus responds to polymixin and terramycin. These newer weapons in combating infection are of inestimable value in the management of staghorn calculi.

THE DECISION TO OPERATE

Once we have assessed to the best of our ability the reasons why staghorn calculi have developed in our patient, we are ready to consider what is to be done about the situation. The first question to answer is concerning the advisability of surgery. We may start in by saying that we have encountered patients with bilateral staghorn calculi who have minimal symptoms and after due consideration of all the factors involved it has been our feeling that they should be managed medically rather than surgically. From the point of view of surgical technique, it is quite possible to split the kidney adequately for complete removal of a solid staghorn stone. Appropriate measures may then be taken to minimize the chance of recurrence, and after successfully carrying this out on one side, it may be repeated on the other side. Several factors, however, should give one pause before setting out on such a course. If the kidneys have been previously operated upon and the staghorn calculi are recurrent the technique of operation is far more difficult and not to be undertaken lightly. If the stone is not solid but consists of multiple separate calyceal stones, or if it is of the friable or mushy calcareous variety, it may defy all reasonable attempts at complete removel. If the patient is a poor surgical risk for unrelated reasons, it must be remembered that two major surgical assaults are required. One may do well to advise the patient that the disadvantages of surgical removal outweigh the advantages and that medical management should be attempted first. If symptoms become too disturbing, it may later become mandatory to embark upon surgical removal.

The surgical approach to the problem is the one of choice when symptoms are marked, when there is evidence of rapid progression of the disease, or when there is accompanying infection. If one kidney alone is involved, one must decide between removal of the calculus and removal of the kidney. This is not always a simple decision. Nephrectomy is usually safe, rapid, and attended by complete recovery. It may therefore be the procedure of choice when the patient is elderly, when the chances of complete surgical removal of the stone are not optimal, or when there is a valid financial objection to a long-drawn-out hospitalization and intensive aftercare. It may also be the most feasible approach when the stone is recurrent after prior attempt has been made at removal. The factor which militates against simple nephrectomy is the fact that a stone may possibly develop in the hitherto normal contralateral kidney. We have seen this happen. In the elderly patient, one does not attach so much importance to this, and the other factors enumerated may be reasonably easy to evaluate except for the financial factor. We feel that this is a very real consideration. For a simple nephrectomy our average patient is discharged from the hospital on the tenth postoperative day and may return to almost any type of employment short of heavy physical labor, in about one month. There is no necessity for numerous follow-up urological studies, treatments, or x-rays. For these reasons, hospital expenses, professional charges, and lost wages are all kept to a minimum. This must be contrasted to a relatively prolonged hospital stay when the kidney is opened, cleaned out, and intubated. The return to work is usually delayed, and the necessity for frequent recheck visits to the urologist, for cystoscopic treatments, and for follow-up x-rays is obvious. It is not sound medical judgment to be swayed unduly by financial considerations, but when a decision is to be made between radical removal and conservative repair, it is only fair to the patient to make clear the economic aspects of the choice. It is to be stressed, however, that when a patient has developed one staghorn calculus and has lost a kidney thereby, it is increasingly important for him to remain under close medical supervision with respect to the remaining kidney. Regular urinalyses and periodic plain films of the renal area become mandatory if early involvement of the solitary kidney is to be detected in time to be helpful.

When one has made decision to perform conservative surgery—that is, to remove the calculus and conserve the renal parenchyma, one must decide on the order of events; in bilateral cases, the degree of parenchymal destruction, the presence or absence of infection, and the amount of discomfort ascribable to each side. No rule of thumb, applicable to all cases, can be formulated. A few examples may illustrate the elements of the problem.

M. S. had a large calculous pyonephrosis on the right side, with some small amount of renal function as measured by dye excretion. On the left, there was a large lower calyceal branching calculus which caused virtually no pain. We elected to remove the stone-bearing lower pole of the left kidney first. When this was satisfactorily accomplished and we were left with a well-functioning stone-free left kidney, we then felt free to do a nephrectomy on the right side, since the salvage value of that kidney seemed negligible. This philosophy, however, carries its perils. Another case in which the same plan was adopted turned out less favorably. The right kidney contained a large staghorn stone but appeared to have better function and more parenchyma than the left which also contained a large stone. With the idea of reconditioning the better kidney first, operation was carried out and the postoperative course was complicated by severe infection and hemorrhage so that a nephrectomy became mandatory. The patient thus lost the better of two diseased kidneys and is now living, fortunately quite comfortably, on one impaired kidney which still contains its calculus. Since we must be realistic and admit that in such surgical procedures there is an ever-present risk of complications which may force nephrectomy, we must give weight to this possibility in our planning. In general, when it appears ideal that each kidney should be cleaned out, it impresses us as better judgment to do the less damaged kidney first. If this is carried out successfully, as it generally is, then whatever happens on the other side will not be disastrous. If the reverse plan is carried out and the poorer kidney is treated first, one may still be in considerable peril when operating on the second side. In any event, there is a calculated risk. The presence of severe pain from one side or the other, of course, will usually dictate that this side be handled first.

SURGICAL TECHNIQUE

Adequate exposure is the sine qua non of successful conservative renal surgery. There is little need to fear generous incisions into the renal parenchyma to allow total removal of calculi and we have stressed elsewhere our conviction that massive through and through sutures for closure sacrifice too much of renal tissue that we are attempting to save to be justifiable. If one achieves complete removal of the calculus from the kidney, it would seem to be wise to utilize nephrostomy tube drainage with a splinting ureteral catheter in order to permit irrigation of the pelvis postoperatively with appropriate solvent solutions and such antibiotics as may be indicated by cultural studies.

POSTOPERATIVE CARE

Preoperative urine cultures will have identified the type of organism which is present in infected cases. It is our practice to institute appropriate antibiotic or chemotherapeutic treatment just prior to operation. Since there is almost certain to be a period of a day or two during which the medication cannot be taken orally, we prefer to use parenteral administration. Penicillin, chloromycetin, or terramycin are particularly adaptable. In addition to parenteral administration, we have also found it helpful to use direct instillations of such solutions as terramycin or polymixin through the nephrostomy tube in the more severely infected cases. We have also used constant or intermittent irrigations of solutions calculated to dissolve any calcareous debris which may have been left behind at operation. Since we are ordinarily dealing with calcium phosphate stones, the solution which we normally use is solution G made up in 1:20,000 zephiran. If solution G proves to be too irritating to the pelvic mucosa, we change to solution M. It will be readily understood that our use of the nephrostomy tube is more as an avenue of approach to the kidney than as a means of drainage.

The length of time over which a nephrostomy tube and splinting catheter is left in place is, obviously, subject to the requirements of the individual case. If ureteropelvic plastic revisions have been carried out, the splinting catheter may be left for 3 or 4 weeks. If no such procedure has been necessary, the tube is removed as quickly as the urinary drainage bespeaks recovery of the kidney.

At the same time, we place the patient on a relatively low phosphorous diet and institute the aluminum hydroxide regimen described by Shorr. This sometimes complicates postoperative bowel regulation, since the aluminum hydroxide is constipating, but this can ordinarily be handled satisfactorily with mild laxatives.

In short, every measure which promises to assist in minimizing recurrence is promptly instituted.

MEDICAL MANAGEMENT

The essential elements of medical management of staghorn calculi have been touched upon while discussing postoperative care. When used in place of surgical excision of the calculi, they become perhaps even more important. The spontaneous disappearance of a staghorn calculus formed during a long period of recumbency has been reported, but it must be admitted that, in general, we are not sanguine enough to hope for complete disappearance of the calculi. Our aim is, if possible, to check further growth of the stones and, if luck is with us, to achieve some decrease in size.

It is especially helpful in medical management if the composition of the stone may be ascertained. When no stone fragment is available for actual analysis, it is necessary to infer the composition from reports on the character of the crystalline sediment of the urine. The overwhelming majority of cases, however, will prove to be calcium phosphate stones, perhaps with admixtures of a few other ions such as ammonium, magnesium, or carbonate. In such cases, the absence of infection and the ability to acidify the urine may permit the utilization of an acidification regimen coupling the acid-ash diet with ammonium chloride, sodium acid phosphate, or some similar agent. When urea-splitting organisms are present, making it virtually impossible to acidify the urine of the renal pelvis, it is unwise to pursue such a course of treatment since under these circumstances, no calcium salts are dissolved and the effect is merely to make more calcium ion available for precipitation. In the patient with poor renal function and a tendency toward azotemia and acidosis, the latter condition may be aggravated by such treatment.

It is more productive, in our experience, to use the aluminum hydroxide routine. Basaljel, which has been especially designed for this purpose, is excellent when well tolerated, but almost 50 per cent of our patients have been unable to overcome nausea and vomiting. Most of these patients, however, prove capable of taking amphojel in adequate amounts. It is our practice to use 40 cc per dose 1 hour after meals and at bedtime. This effectively decreases the amount of phosphate ion available for precipitation in the urinary tract. In a few cases, we have also used estrogens, as advocated by Shorr, to increase citric acid output in the urine, but we do not feel qualified to pass on its value. We are firmly convinced, however, that the aluminum hydroxide routine is of real virtue. In our case which has been followed the longest, we have had dramatic proof of its efficacy. This patient had bilateral staghorn calculi and each kidney had been surgically cleaned out, but had become refilled with stone before we saw her first. Because of pain in the right renal region, we did a second right nephrolithotomy in December 1946. Despite all our precautions, we were horrified to see a minute fleck of stone begin to grow rapidly. When we first became aware of the work of Shorr, we instituted aluminum hydroxide therapy with estrogens. The rapid growth of the stone ceased and as long as she was on this treatment, the size remained constant. Therapy was stopped because of menorrhagia and metrorrhagia and marked constipation, but as soon as the treatment was discontinued, the stone resumed its growth. Treatment was started again and stone growth stopped. Over the years, for one reason or another she has discontinued treatment from time to time. Each time she stops the aluminum hydroxide, the stone starts growing, but while on therapy, it stays substantially the same in character. We have since had numerous other demonstrations of the fact that this routine, which is subject to numerous objections and shortcomings, is an effective measure in the medical management of stone.

It has been our experience that when stone and infection co-exist, there is nothing to be gained by attempting to eradicate infection without removing the stone. It is perfectly true that in acute flare-ups of pyelonephritis, with evidence of extension of the infection, the appropriate antibiotic or chemotherapeutic agent should be given liberally, but in the absence of such acute situations, it does no significant good to administer these medications. It is better to reserve them for such time as surgical removal of the stone may be attempted.

Finally, it is to be stressed that a high fluid intake constitutes a valuable element of stone control. The patient is urged to make a habit of taking water far in excess of the dictates of thirst in order that stone-forming substances may be kept in solution and carried on out of the urinary tract without precipitation.

In the smaller number of cases in which staghorn stones are composed of other substances than calcium phosphate, we do not employ the aluminum hydroxide routine but follow the simple dictates of time-honored dieting and medical management of stone: Alkaline ash diet and sodium citrate for uric acid stones, diet low in foods of high oxalic acid content for oxalate stones, and so on through the roster. In these instances, the medical management seems less likely to be satisfactory.

We have found it most helpful to take the time to be explicit to our patients concerning the nature of their difficulties, to show them their stones in the x-ray films, and to point out to them any changes in size which occur during the course of therapy. We have felt that they become more zealous in their pursuit of our directions and more faithful in reporting for follow-up care. Lastly, and perhaps most important, they become more understanding and co-operative whenever it appears that ground is being lost under a medical regimen and surgery must be embarked upon.

SUMMARY

The complex factors in the management of patients with unilateral or bilateral staghorn calculi of the kidneys are reviewed. First, it is necessary to assess the etiological factors such as heredity, metabolic defects, urinary stasis, and infection in order to determine the proper therapeutic approach.

Second, it is well to consider the possibility of medical management of the disease as a substitute for surgery in certain types of cases.

Third, when surgery is decided upon, radical nephrectomy or conservative removal of the calculus may be possible alternatives. The choice is determined by the amount of renal damage, the degree of functional integrity, the status of the contralateral kidney, and certain economic considerations of importance. In bilateral cases, the order of events must be planned with proper caution.

Fourth, immediately before and after surgical removal of these calculi, it is of the utmost importance to employ every reasonable measure to insure against recurrence. These measures are dissolution of any possible remaining calcareous fragments, and a vigorous assault on infective organisms, plus appropriate dietary and medical treatment.

Fifth, the principal elements in the medical management of calculous disease are to be applied not only to those patients in whom surgery is regarded as undesirable, but also to those patients who have been subjected to nephrolithotomy.

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EXPERIMENTAL UROLITHIASIS VI. FAILURE OF HYALURONIDASE TO INHIBIT GROWTH OF STONES ON FOREIGN BODIES IN THE RAT

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Butt and Hauser[1-4] recently have reported some interesting observations on urinary colloidal activity that may have some bearing upon stone formation. Urinary colloidal activity was investigated principally by ultramicroscopic examination in which the number of particles exhibiting Brownian motion was estimated under the darkfield microscope. Using this test, as well as others, it was found that urine obtained from Negroes generally exhibited higher colloidal activity than urine from white subjects. This finding was used as a possible explanation for the lower incidence of urolithiasis in the Negro. A similar difference was observed when the urines of pregnant and nonpregnant females were compared, apparently corresponding to the relative protection from stone formation which is said to occur during pregnancy. It is also interesting to note that in stone-formers the urinary colloidal activity was in general below the average for patients who were not suffering from calculous disease.

It was observed that the administration of hyaluronidase to human patients resulted in an increase in the colloidal activity of the urine as judged by the same tests. It was therefore concluded that hyaluronidase might be a rational treatment for patients with urolithiasis. When so treated, 80 per cent of the cases studied responded with a significant increase in the urinary colloidal activity.

Although these findings indicate that hyaluronidase produces changes in the colloidal activity of the urine, there is as yet no satisfactory clinical data to suggest that such colloidal changes alter the process of stone formation. The following experiment was done to test the effectiveness of hyaluronidase in preventing stones in rats, where the stimulus to stone formation was the presence of a foreign body in the bladder. The same method has been used to demonstrate the effect of several other factors on stone formation and found to yield satisfactory results as has been previously reported.[5-8] It was hoped that by using this

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[6] Grove, W. J., Vermeulen, C. W., Goetz, R. and Ragins, H. D.: Experimental urolithiasis II. The influence of urine volume upon calculi experimentally produced upon foreign bodies. J. Urol., 64: 549, 1950.

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test hyaluronidase would be found to influence the growth of stones and thereby substantiate the reasoning of Butt and Hauser. Since the test could be subjected to control, the conclusions arrived at, if positive, would lend support to the clinical use of hyaluronidase.

METHODS

In general, the method used in this experiment was the same as that described in previous publications. Male white rats weighing 150–200 gm. were operated upon and a foreign body inserted into the bladder by suprapublic cystotomy. The foreign body in each instance consisted of a small rectangular piece of sheet zinc about 3 mm. in length. The animals were fed a normal rat diet composed of Purina fox chow. On this diet calculi are not formed spontaneously, but if a foreign body be present in the bladder, a stone composed of magnesium ammonium phosphate is produced about it.

TABLE 1. *Summary of results*

	NUMBER OF RATS	AVER. pH OF URINE	AVER. WT. OF CALCULUS IN MGM.
Controls	20	6.2	37.2 ± 7.9 (S.E.)
Hyaluronidase	22	6.4	45.1 ± 7.1

A total of 50 animals, each with a foreign body in the bladder, was used in this experiment. Half of them were treated with hyaluronidase while the remainder served as controls. The hyaluronidase was injected subcutaneously in the abdominal wall, the injections being given once daily, 6 days a week, for the entire 6 weeks of the experiment. For each injection the hyaluronidase was contained in 0.2 cc of physiological salt solution. In 12 of the animals, 5 turbidity reducing units of hyaluronidase (Wydase) was used for each dose, while in the other 13 animals, 15 TR units were given. The control animals received no hyaluronidase but instead were given a daily injection of 0.2 cc of physiologic salt solution.

At the end of 6 weeks the bladders were exposed and urine was aspirated for pH determination and culture. In each instance the amount of stone that had formed was then determined by weighing the stone and subtracting the initial weight of the foreign body.

RESULTS

In five of the 25 rats in the control group, accidental infection occurred. The results in these animals were therefore discarded to avoid the introduction of another variable in the experiment. Of the animals treated with hyaluronidase, three of the 25 were found to be infected at the completion of the experiment; these also were discarded. There appeared to be no significant difference in the urinary pH values of the animals treated with hyaluronidase when compared to the controls. There was also no significant difference between the two groups in either the number of animals developing stone or in the average amount of stone produced. Of the 20 animals in the control group, 16 had a calculus deposit upon the foreign body of over 10 mg. as compared to 21 of the 22 animals in the group

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treated with hyaluronidase. The average weight of stone produced in the 20 control rats was 37.2 mg., while in the 22 animals treated with hyaluronidase, the average weight was 45.1 mg. Since the amount of stone produced in the hyaluronidase-treated animals was approximately the same under both dosage schedules, the results have been combined in table 1.

DISCUSSION

In this experiment hyaluronidase entirely failed to prevent stones. Indeed, on the average, somewhat more stone was produced with hyaluronidase than in the controls, though this difference is of no statistical significance. The amount of hyaluronidase administered would appear to be sufficient since when calculated weight for weight the dose was 10 or 30 times that recommended for human beings.

The real question arises when we consider whether or not these experimental results refute the claims made for hyaluronidase in clinical patients. To account for our negative findings, several possibilities may be considered. It may be that in the rat hyaluronidase does not produce the urinary colloidal changes observed in human beings. No observations on the colloidal activity of the urine in the rat are available, however. It may also be objected that by the use of a foreign body the action of hyaluronidase is in some way antagonized or sidestepped. It will be remembered, however, that for most of the time in these experiments the urine was not bathing a foreign body but was rather in contact with a stone that had formed an encasement around it. Consequently either hyaluronidase becomes ineffective in the presence of a stone, or the foreign body, even though buried in a stone, is still able to antagonize the action of hyaluronidase. This latter possibility seems unlikely to us. Finally, hyaluronidase may have failed to inhibit stone formation because its action was over-powered by the strong stimulus provided by the presence of a foreign body in the bladder. These experiments may therefore mask possible action by hyaluronidase. In this connection it may be said that in previous papers several methods have been described that are capable not only of preventing stone development on a foreign body but even of dissolving previously formed stones.

In view of these possible objections, our experiments cannot be taken as invalidating the notion that hyaluronidase prevents stones. Unless hyaluronidase can be shown in other types of experiment to exert a preventing effect, we will have to await the results of observations on a sufficient number of human patients with adequate controls before a satisfactory statistical evaluation of its effectiveness can be made.

SUMMARY

It has recently been suggested that hyaluronidase may be an agent capable of inhibiting urinary stone formation. This experiment was done to test the effectiveness of hyaluronidase in preventing the development of stones around foreign body nuclei in the bladders of rats. Daily injections of hyaluronidase were given to one group of rats and the amount of stone formed around the foreign bodies was compared to the amount formed in another group of control rats not receiving hyaluronidase. Stone production in the 2 groups was essentially the same, indicating that at least in this type of experiment hyaluronidase is without effect.

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SEPTIC INFARCTION IN ONE KIDNEY AND ECTOPIA OF THE OTHER

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We recently have had occasion to study a clinical case which we have decided to publish because of its exceptional interest.

The patient was a 70-year-old woman, a widow, born in Valdepeñas, where she lived. There was little personal background history. At the age of thirty she had a febrile process with high temperatures and sudden rises, which persisted throughout three months and was diagnosed as malaria. Later, she had only suffered from pyorrhea with frequent gum abscesses and apicular granulomas. She had had several normal pregnancies.

The trouble for which she consulted us began after she had had acute gingivo-alveolar suppuration, about forty days before we saw her. In these circumstances, a febrile picture set in. The bouts of fever were preceded by violent shivering and followed by profuse sweating. There were sudden rises of the temperature to 104F, accompanied by pain in the right lumbar region. Without any accurate diagnosis, which was impossible since she lived in the country, she was ordered treatment by penicillin, streptomycin, and sulphodiazin, and was given 10 m. units of the first and 10 gm. of the second in the time mentioned. The fever graph was only slightly modified and the general septic condition became more marked again. She had a bout of anuria which lasted three days. In the many analyses which were done in this time, a marked leukocytosis always was found (with an average count rate of 20,000), intense polynucleosis (from 89 to 94 per cent), a very high sedimentation rate, and a blood urea rate of 0.62 gr.

In these circumstances, one of us (F. V. D.) saw the patient for the first time. He found her obese, plethoric, virilescent, sweating profusely and with a high temperature (104.3F). No anomaly whatever was found in the respiratory system. In the circulatory, tachycardia was found (102 p.m.) with hard and flexuous arteries, a systolic murmur in the second right intercostal space (aortic focus), of atheromatous type, and normal blood pressures (140 80). All the rest of the examination was negative, but for slight pain on palpation at the inferior pole of the right kidney (costolumbar and subcostal points), which became more marked when breathing deeply.

In view of the "needle" type of fever and the renal localization of the only examination datum, he gave a hypothetic verdict of possible renal infarct, which was almost certainly septic, and requested the collaboration of the other author, the urologist (T. de la M.), who ordered the necessary examinations and tests. A thorax radiography done to make sure there was no pathological focus that might have similar clinical manifestations and to discover any disorders that might be related to a renal process, proved normal, showing only the natural signs of plethoric constitution.

In the clinical examination, apart from the aforementioned pain, a slight left concavity of the column was found and the psoas line was missing on this side.

Excretory urography: At the end of 7 minutes, we saw the right pelvis slightly faulty with unclear contour. No elimination was observed on the left side. The bladder gave a normal contrast. At the end of 15 minutes the images were as before. See figure 1, *A* and *B*. This pyelographic study enabled us to suggest a diagnosis of aplasia of the left kidney or perhaps autonephrectomy due to the septic process suffered by the patient when she was thirty. But subsequent examinations set the problem in another way.

By chromocystoscopy we found a vesical capacity of 300 cc, with a sound mucosa, the right ureteral orifice like a vaulted niche, with a strong elimination of blue at the end of four minutes. After 9 minutes, there was weak and dribbling elimination on the left side. In view of this, we thought it indispensable to do bilateral catheterization, which was carried out. A catheter passed on the right side without any difficulty up to 15 cm., with rhythmic ejaculation. On the left side, an obstacle appeared at 9 cm.; this was overcome, and there was continuous elimination, accentuated on exertion. In 30 minutes we collected 10 cc on the right side and 30 cc on the left. These facts indicated the necessity of retrograde pyelography, which was done with 8 cc on the right side and 12 cc on the left.

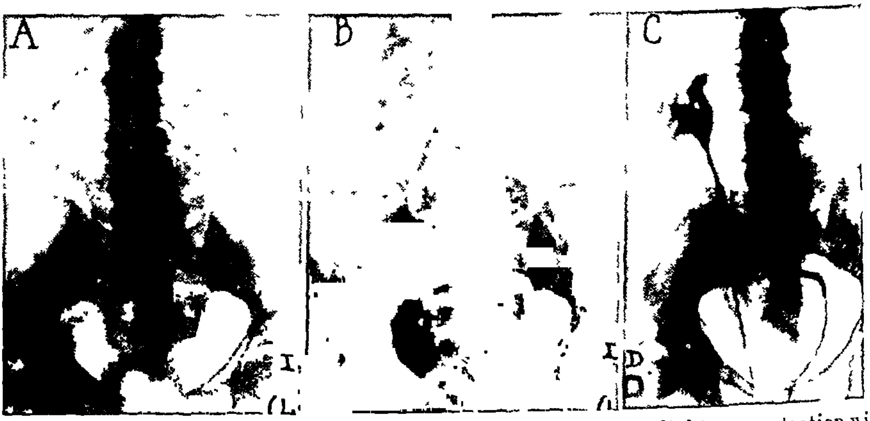

FIG. 1. *A*, excretory urogram. Left side negative. Right side, slight concentration with faulty pelvis (film after 7 minutes). *B*, excretory urogram. Absence of elimination persists on left side. On right side, slight increase of concentration. *C*, retrograde pyelogram. Left kidney ectopic with bifid hydronephrosis. Right kidney in first degree ptosis. Reflux of large collectors in middle calyx (infarct zone).

Examination of the catheterized specimen from the right kidney: urea, 17.5 gr. and chlorides, 6 gr., with abundant cells and erythrocytes, but without germs. Left kidney: urea, 8.2 gr.; chlorides, 3 gr., cells and erythrocytes without pyocytes or bacteria.

Bilateral retrograde pyelography (supine): Left kidney, ectopic, with bifid hydronephrosis. Right kidney, festooning of the lower and middle calyx with infiltration of opaque material in the corticomedular zone. The films taken with the patient erect showed only a slight right displacement, where a greater infiltration of the opaque material was seen in the lowest third. See figure 1 *C*.

The ensemble of data from the urological examination allowed us to draw the conclusion that the clinical picture was due to infarctation of the right kidney, and the subsequent confirmation of this seemed highly interesting to us. There was ectopia of the left kidney with normal functioning at the latter, which does not permit it to be diagnosed as pathological.

In face of the patient's septic picture and clinical refractoriness to antibiotics we decided to operate. After the patient had been suitably prepared and spinal anesthesia done, an ample lumbotomy was carried out and after some 15 cm. of fat had been cut through and the renal capsule was reached, and Gerota's zone, we easily freed all the renal surface, except the lowest third and the middle one, where the capsule was found adhered. On its being separated, an area of some four square centimeters was found to be blackish brown in color, fluctuating and macerated. Puncture of this only enabled us to extract a muddy exudate. The thickness of the infarct, determined by the depth at which the needle stopped extracting fluid, was about 3 cm. The rest of the parenchyma appeared absolutely normal. The fluid was extracted for bacteriological analysis. Electrocoagulation of all the damaged area was done, a drainage outlet being left and the area being closed at three levels.

The extracted hemorrhagic fluid proved totally sterile, no germ grew in it and only organic detritus and parenchyma residues appeared.

The postoperative course was excellent. Twelve hours after the operation, the temperature had dropped to 100.4F and in 36 hours it had gone down to 97.7F, without any fresh rise.

The patient was discharged as cured 7 days later.

COMMENTS

One of the authors (T. de la M.) has so far had occasion to study 3 cases of kidney infarct, including this one. All three were quite different in all respects. The first was a case of genuine anthrax, with the edges eaten away by the pathological virulence of the local affection, and the clinical circumstances of the case made nephrectomy indispensable. The second case was one of perinephritis which, after being operated on, continued to show a highly septic febrile picture. A suppurating renal cavity was found at the next operation. The extension and depth of the anatomical lesion also caused renal enucleation.

In the first 2 cases, which occurred before the advent of antibiotics, the clinical picture seems to have possessed a septic gravity which the present case must have lacked, for it was treated a long time with enormous doses of penicillin and yet gave an invariable septic picture. The absolute negativity of cultures of the fluid from the puncture of the infarct and the preparations studied, proves that the antibiotics were useful, since they sterilized the infarctic focus. But, nevertheless, they hardly modified the clinical picture, which persisted in the same febrile form, and with the same bad general condition and biological reaction (leukocytosis, polynucleosis, high sedimentation rate, etc.). This clinical fact allows us to establish two inferences: First, that septic lesions of the kidney may continue to give a clinical picture of a clear septic appearance when they have already become sterile, a thing we can only attribute to one of the two following causes: A) to a reaction of the organism following the reabsorption of the detritus and products of the local autolysis; B) the passage of oxine into the blood. Second, that if, as experience proves in the other systems of the organism, antibiotics can modify the clinical pictures and sometimes mask a syndrome with the appearances of a cure or improvement which does not actually exist, in other cases, like the one here surveyed, even when they sterilize the lesion they do not alter the clinical picture, which, for other— but no longer septic — reasons, continues to display the same signs of malignancy and apparent infectiousness. This fact is very telling in these septic lesions of the renal parenchyma and no other organ of the body can, perhaps, bear comparison with the kidneys in this respect. In the same way, it may be thought that some clinical pictures which are sometimes attributed to bacterial resistance to antibiotics are due to a similar cause as that of our case here set forth. So it results that

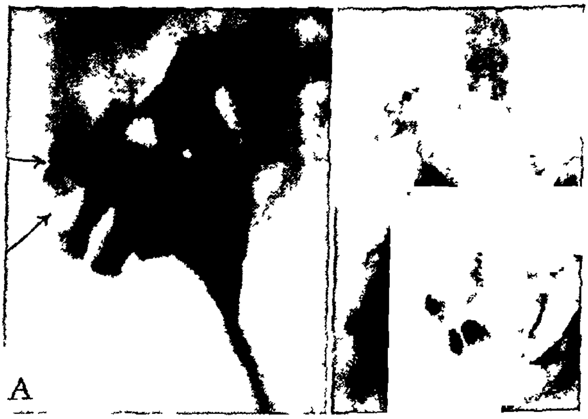

Fig. 2. *A*, excretory urogram of normal size. Evident proof of infarcted zone by festooning and blurring of contours. *B*, excretory urogram with 45 degree inclination plane. Affected zone is blurred and opaque material perceived between medullar and cortical areas.

antibiotics can sterilize a septic renal infarct and even prevent its turning into perinephritis, but they may not modify a clinical picture which can only be corrected by other means (surgical ones).

It is impossible to establish the pathogenetic nature of the infarct. It seems to us excessive to attribute a definite "clinical morphology" to infarcts according to whether they are arterial, venous, or traumatic, as Regan and Crabtree (1948) advocate. In the first place, because this precise delimitation of the anatomical morphology is somewhat questionable and, above all, because we do not see a single datum which may have a pathognomonic significance of each type of renal infarct, since the clinical data for the simple diagnosis of infarctation are also questionable. Neither the renal function tests, nor the excretory urographic images, nor the analytical findings in the urine (unilateral bacteriuria, albuminuria, or hematuria, etc.), nor much less even the clinical picture can give us guidance that is beyond discussion. If in this case we had tried to diagnose on the strength of the first pyelographic study or the chromocystoscopy, we should not have succeeded in diagnosing the renal ectopia nor clearly seen the existence of a renal infarct. Perhaps we should not have operated, either, because of the functional inexistence of the left kidney and because we believed that the diseased kidney was the ectopic one since the concavity of the spine was on this side. Even normality on examination cannot be taken as excluding the possibility of renal infarctation.

From the etiological standpoint we cannot come to definite conclusions. In this case. the generalized arteriosclerosis and the multiple foci in the gums and dental granuloma with which the patient was affected may have been the cause of the process through a simple bacteriemia, as happens in the majority of extrarenal infections, however distant they may be.

The radiological study is much more important to us. The existence of festooned zones in the pyelographic opaque material, in the ascending image, in the cortical or medular region or both, by reflux of the large collectors, may provide a diagnostic datum of renal infarct (fig. 2). We believe that the presence of this datum in association with a septic clinical syndrome of possible renal localization ("needle" fever of "urinous" type, lumbar pain, characteristic concavity of the dorso-lumbar column,—Mathé's or Chevassu's signs—) may give the diagnostic key to a renal infarct.

There is one therapeutical consideration which our present case calls for. Up to now, total or partial nephrectomy is systematically done, as seen in the above-quoted review of Regan and Crabtree. The absolute cure achieved in our case by electrocoagulation. with disappearance of the fever in 36 hours' time and the normalization of all the clinical phenomena, allows us to advise this practice in all similar cases. especially when, after a prolonged and intensive use of antibiotics and chimiotherapics, it is suspected, and possibly confirmed, by means of a frottis, that the infarct is sterile. We shall be told that we can never absolutely assert that an infarct is sterile, and that haste in operating precludes the adoption of attitudes which might be dangerous: but with all the antibacterial means now at our disposal, this attitude can be advocated as regards future cases as conservative therapeutics of the kidneys.

CONCLUSIONS

We present a clinical case of right renal infarct with ectopia in the left kidney, in which diagnosis was done on the clinical picture and the radiological image. As regards the existence of ectopia in the other kidney, the noninfarcted one, the complementary urological tests gave results which might have lent themselves to confusions. The authors consider the localized festooning of the pyelographic opaque material as of almost pathognomonic value. They draw attention to the fact that a clinical picture of clear septicity persisted in an infarct which had been made sterile by the previous treatments with antibiotics. For similar cases that are very much localized and suspected of being sterile, they advise electrocoagulation instead of the classic nephrectomy.

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ANEURYSM OF ACCESSORY RENAL ARTERY

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In recent years more and more frequently aneurysm of the renal artery has been recognized and treated as a clinical entity. It has become possible to diagnose this condition because of specific radiographic changes. Nevertheless, aneurysm of the renal artery must be considered as a relatively rare disease since less than one hundred cases have been reported in the literature.[1] In this paper an additional case report of aneurysm of a renal artery is being presented for two reasons: 1) The clinical diagnosis of aneurysm was made possible because of specific radiographic changes; 2) The aneurysm subsequently proved to have occurred in an obliterated accessory renal artery.

CASE REPORT

A. G., a 40 year old white man, was admitted to the Mt. Auburn Hospital, July 12, 1951 because of dull pain in the left upper quadrant. He had had no previous urinary symptoms and had enjoyed good health. At the age of eighteen, following a severe streptococcus infection of the right middle ear, the patient noted the appearance of multiple "purple spots" on the nose, lips, and ears. A possible significant fact brought out in the family history was that his mother had experienced repeated, severe nose bleeds since childhood. Telangiectases of the nasal septum were found to be the source of these hemorrhages.

Physical examination disclosed a well developed and nourished adult male. On the distal half of the nose, the cheeks, the chin, and the mucosa of the lips there were multiple, punctate, bluish-red spider nevi. The heart and lung fields were normal. Blood pressure was 134/76. There was moderate tenderness without spasm in the left upper quadrant but no masses could be palpated. The external genitalia were normal, rectal tone was good and the prostate gland was not enlarged.

Erythrocyte count was 3.74 million with 11.6 grams of hemoglobin. White blood count was 10,700 with a normal differential. Blood smear demonstrated slight achromia. Platelets were normal. Hinton was negative. Voided urine specimen was yellow, clear, specific gravity 1.012, no albumin, no sugar, 2–4 red blood cells per high power field, but no pus cells or organisms were found in a methylene blue stain of the sediment. Culture of the bladder urine was sterile. The nonprotein nitrogen was 33 mg. per cent. Test for occult blood in the stool was negative.

Excretory urograms on the day after admission revealed prompt excretion and good concentration of the dye with a normal filling of the calyces, pelves,

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Read at meeting New England Section, American Urological Association, Boston, Mass., November 8, 1951.

* Deceased December 13, 1952.

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and ureters. A circular area of calcification, 2 cm. in diameter, could be seen just in front of the lower pole of the left kidney at the level of the second lumbar vertebra (fig. 1, *A* and *B*). A lateral view identified this ring to be anterior to the renal pelvis (fig. 1, C). Laminograms placed this shadow in the same plane as the kidney pedicle. Although a calcified lymph gland could not be excluded, it was believed that the patient had an aneurysm of the renal artery.

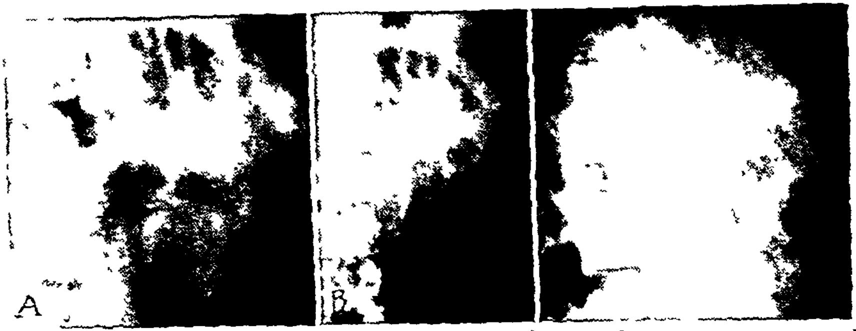

FIG 1 *A*, plain left urogram demonstrating "ring" shadow. *B*, excretory urogram with "ring" shadow outside left renal pelvis *C*, lateral view demonstrating "ring" shadow anterior to left renal pelvis

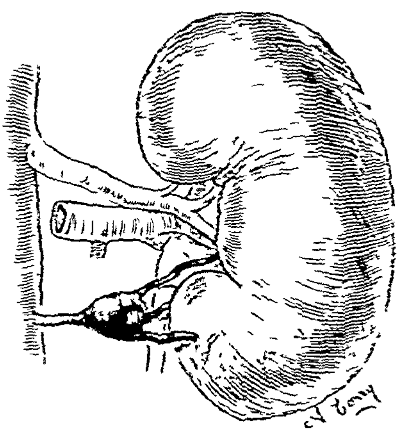

FIG 2 Diagrammatic drawing of normal kidney and accessory artery with aneurysm

On the fourth hospital day catheterization of each ureter was carried out and individual kidney functions determined. Phenolsulfonphthalein appeared in 3 minutes with a 15 per cent concentration in 15 minutes bilaterally.

The patient's symptom of pain in the left upper quadrant subsided on the second hospital day and did not recur. However, in view of the calcific shadow in the urograms, a diagnosis of aneurysm of the renal artery was strongly supported and surgery advised. Operation was carried out on the seventh hospital day. Renal exploration was performed through a left flank incision. After mobilization of the kidney the calcified structure anterior to and below the renal pedicle

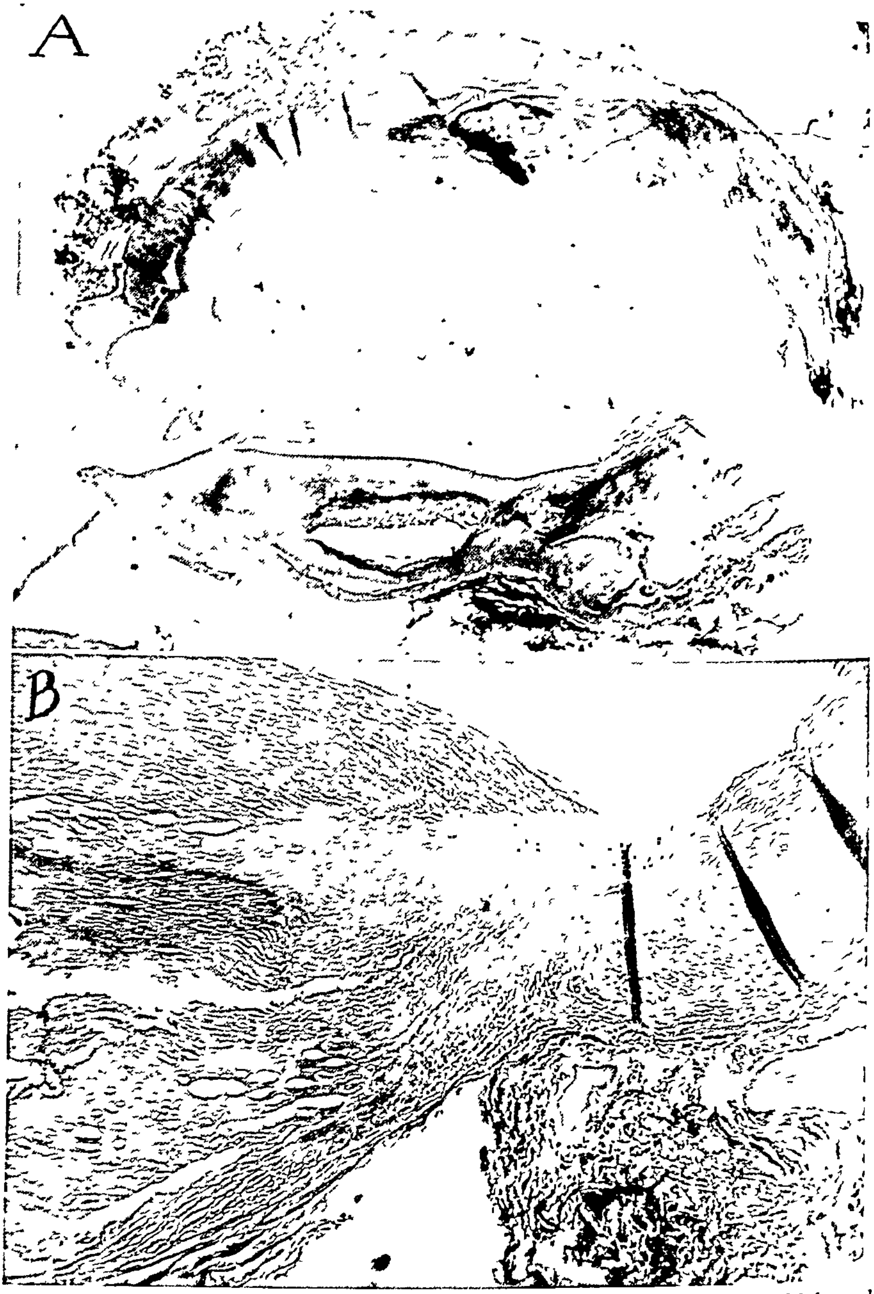

FIG. 3. *A*, photomicrograph of aneurysmal sac after decalcification. Note thick media and internal elastic membrane. × 12. *B*, internal elastic membrane and muscular media are well delineated. × 100.

was readily isolated and found to be entirely independent of the main renal artery (fig. 2). The calcified mass did not pulsate. It consisted of a main afferent channel and several efferent branches having the consistency of blood vessels.

These channels were ligated and divided but no blood was found to course through the lumina. The calcified structure was then removed.

The operative incision was then closed with drainage. The patient's postoperative course was uneventful and he left the hospital on the eighth day after surgery, asymptomatic.

The pathologist, Dr. H. Edward MacMahon, reported the following: "The specimen consists of a cystic structure measuring 1.5 by 1.5 by 0.7 cm. At one point there is a small opening through which a probe can be passed and a hollow lumen discerned. On cut section the wall of the specimen is focally calcified. Histological study after decalcification demonstrates that the wall of the cystic structure is that of a poorly formed necrotic vessel (fig. 3, *A*). The better preserved areas show a thick media of smooth muscle cells and a prominent internal elastic membrane (fig. 3, *B*). Calcification and atherosclerotic changes have destroyed a good part of the wall of the vessel. There are no blood cells in the lumen of the structure."

The histologic diagnosis was aneurysmal dilatation of a poorly formed artery with secondary degenerative changes and calcification. At the time of surgical removal the vessel was not functioning.

DISCUSSION

The occurrence of an aneurysm in an accessory or polar renal artery is indeed a rare condition. Polar renal vessels occur in about one in seven kidneys, the inferior polar vessels sometimes causing ureteral obstruction. No obstruction was present in the case presented.

Aneurysm of the renal artery when calcified usually forms a ring-like shadow with a radiolucent center and a periphery which may or may not be entirely calcified. Lateral x-ray views demonstrate that the calcified ring of an aneurysmal sac is anterior to the renal pelvis. Laminograms are often of value in fixing the ring shadow to be in the same plane as the kidney pedicle. X-rays in this case demonstrated the calcific shadow to be nearer to the lower pole of the kidney whereas the normal renal artery enters the hilum at the center of the kidney. At operation the low position of the calcified ring was demonstrated to be due to the occurrence of the aneurysm in an accessory, polar renal artery which entered the parenchyma at the lower pole. Since no blood coursed through the vessel and the aneurysm did not pulsate the artery had undoubtedly obliterated itself spontaneously.

Nephrectomy did not have to be performed as the main renal blood supply was intact and the aneurysm was readily accessible and easily removed.

SUMMARY

A case of aneurysm of an accessory renal artery is reported. This case is of unusual interest because the aneurysm occurred in an accessory renal artery which at the time of surgical removal was obliterated and nonfunctioning.

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FRACTURE OF GIANT URETERAL CALCULUS

CARL E. BURKLAND

Giant ureteral calculi (cigar stones of the ureter) are uncommon, but fracture of such a stone in the living patient is still more unusual. We wish to report a case of a giant ureteral calculus in which the history of the stone covers a period of 32 years. A week before we saw the patient, the calculus fractured and caused considerable pain.

CASE REPORT

A. W., a married white woman, 53 years old and an employee of a local air base, was first seen on July 25, 1951, complaining of severe pain in the right side of the abdomen. Family history was noncontributory. Past history revealed good general health with no serious debilitating illnesses or injuries. Tonsillectomy was performed at 24 years of age. In May 1950, a benign calcified duct of the left breast was removed. She had been bothered with chronic constipation and flatulence for several years. There were no urinary symptoms previous to present illness. She has been married 4 times, to the present husband for 4 years. She has one female child, age 32 years, living and well. She has always drunk a considerable amount of water and never much milk or alcohol.

The present illness began in February 1919, when the patient had an attack of severe pain in the right side following delivery of her first and only child in Georgia. The pain persisted along with frequency of urination, and in March of 1919 she was hospitalized. X-rays made at this time revealed some small stones in the lower right ureter. Cystoscopy was performed, but the stones were not recovered. Cystoscopy was then repeated twice a week for the next 3 months, olive oil was instilled into the ureter and she finally passed one small stone. Open surgery was advised, but not accepted.

She got along fairly well afterwards, but would have occasional attacks of back pain once or twice a year until 1922 when she suddenly began to feel much better with no pain or urinary symptoms. She suffered no difficulty until 1943 when she was seized with a severe pain in her right side while in Atlanta, Georgia and was hospitalized. An x-ray revealed a large stone, about 3 inches long, in the right ureter. Surgical removal was advised, but not accepted. She felt better and from 1943 to 1950 had no attacks of pain or urinary symptoms. She was quite active, worked as a clerk and taught folk dancing for many years. In September 1950, she had a plain film of the abdomen taken for a check up and it showed a very long stone in the right ureter (fig. 1, *A*). She was asymptomatic at the time and nothing was done.

Her immediate present illness began on July 18, 1951, which was her wedding anniversary. She went out on a party with her husband and later that evening, while having intercourse with her husband, severe pain developed in the right side accompanied by nausea. Sedatives were prescribed, but the pain persisted,

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and on July 23, 1951, intravenous urograms were made which revealed fracture of a giant ureteral calculus in its mid-position and no function through the right kidney (fig. 1, *B*). The left kidney and ureter appeared normal. The pain in the right side became much worse; cystoscopy was done, but no catheter could be passed up the right side. On July 29, 1951 she was admitted to the hospital. Temperature, pulse and respiration were normal. Blood pressure was 118/72. Moderate tenderness was elicited in the right flank and side, but no masses or organs were palpable. Laboratory data: Hemoglobin, 14.1 gm.; white blood count, 7,600 with normal differential count; urinalysis: albumin, 1 plus, many white blood cells, few red blood cells, few mixed bacteria (Aerobacter coli and Streptococcus faecalis); nonprotein nitrogen, 31.5 mg. per cent; fasting blood calcium, 9.6 mg. per cent; blood phosphorous, 3.4 mg. per cent.

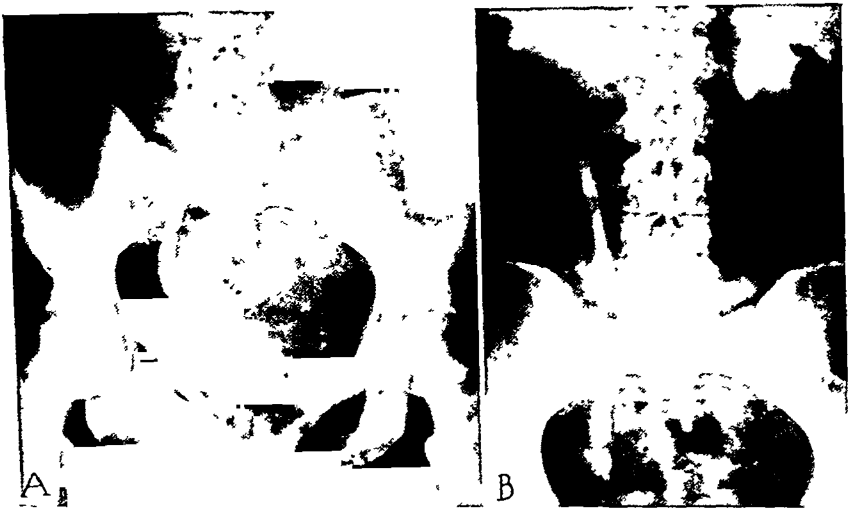

FIG. 1. *A*, plain film showing giant ureteral calculus, 16 cm. long, in right ureter. *B*, excretory urogram showing fracture in midportion of giant ureteral calculus. No function of right kidney but normal left kidney.

Nephro-ureterectomy was advised, accepted and carried out. A small extraperitoneal incision was made in the lower right quadrant to free and isolate the lower half of the ureter. Then the patient was turned with the right side up and through the usual lumbar incision, a hydronephrotic kidney together with a dilated ureter, which was filled with the large calculus (16 cm. long) and a smaller stone were removed in one piece (see fig. 2). Manipulations during and following surgery broke the rather fragile stone into several pieces. She stood the procedure well, her wounds healed per priman, and her entire convalescence was uneventful. She left the hospital on the tenth postoperative day.

Since then she has remained very well and symptom free with clear urine.

Pathological report: The right kidney measured 8.5 by 3.5 by 3 cm. The major portion of the kidney parenchyma was reduced to a mere shell, measuring 0.3 cm. in greatest thickness. The calyces were all dilated and saccular. The ureter was markedly enlarged and thickened and measured 15 cm. in length. Palpable stone was felt running the entire length of the ureter. Upon opening the ureter at the distal end there was found a stone which had been fragmented in two places and when reconstructed, it measured 8.5 cm. in length and 1.2 cm. in greatest diameter. The surface was granular and blackish brown, the broken end revealed a concentric pattern of hard, brownish gray crystalline material. In the upper portion of the ureter a second stone was found which was also fragmented in two places, measuring 7.5 cm. in length and 1 cm. in greatest diameter. The distal portion of the stone was smooth and round and contained a cap of yellowish gray crystalline material covering the major portion of the stone which was brownish in color. The ureter was thickened, focally hemorrhagic, and intimately attached to the stone in the lower portion. The ureter measured 3 cm in greatest circumference.

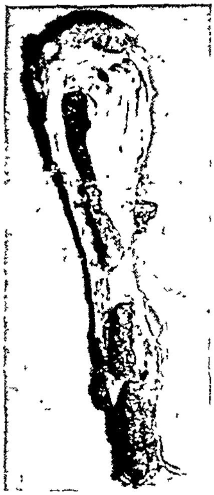

FIG. 2. Photograph of right kidney and entire ureter containing stone

Microscopically, sections from the kidney proper revealed a marked atrophy of renal parenchyma. The majority of the ducts present had the so-called "thyroid appearance" being markedly dilated and filled with a deeply acidophilic colloidal material. The interstitial tissue exhibited marked fibrosis and focal infiltration with lymphocytes. The parenchymal arteries exhibited a marked hypertrophy of the muscle coats. An occasional glomerulus was present which presented a marked hypertrophy of the glomerular tufts. The pelvis of the kidney showed a severe chronic inflammatory reaction and a severe fibrosis.

A section taken through the lower portion of the ureter revealed extensive erosion of the epithelium and compressional necrosis of the underlying tissue. In several areas the transitional cell epithelium was intact, and there was noted a marked squamous cell metaplasia. There was a considerable chronic inflammatory reaction, and the wall showed a marked fibrotic thickening. Analysis of the stone revealed it to be composed of apatite and magnesium ammonium phosphate hexahydrate.

Pathological diagnosis: Cigar-shaped stone of the ureter; chronic ureteritis and ureterectasia with focal squamous cell metaplasia; hydronephrosis; chronic atrophic pyelonephritis, severe.

Survey of the literature reveals rather few reports of giant ureteral calculi. In table 1 are listed the authors and the site and size of the giant ureteral calculi reported by them.

TABLE 1

AUTHOR	YEAR	PATIENT'S AGE AND SEX		URETER	LENGTH OF STONE IN CM.	CIRCUMFERENCE IN CM.	WEIGHT IN GRAMS	LENGTH OF HISTORY IN YEARS
Rovsing	1901	38	F	Left	18.00	—	15.50	6+
Bovee	1905	—	M	Left	7.00	3.85	87.30	—
Israel	1907	31	M	—	17.00	9.00	54.40	4+
Fedoroff.	1909	22	M	Left	19.00	—	52.00	9
Collinson	1913	29	F	Left	12.50	—	50.40	25
				(2 stones)	6.25	—	29.30	
Buerger	1914	26	M	Left	10.00	1.6	—	—
Buerger	1914	55	M	Right	5.30	1.7	—	10
Specklin	1915	48	M	Left	11.00	—	51.00	30
Abell	1916	32	M	Right	7.50	7.00	24.00	—
Peraire.	1916	—	—	—	9.50	—	41.00	—
Ley	1920	—	—	—	7.50	10.00	66.30	—
Kidd	1920	18	M	Right	5.63	3.75	30.00	—
Heath	1922	30	M	Left	15.00	7.80	65.80	4+
Tennant	1924	78	M	Left	5.00	6.00	66.00	—
Reshower	1927	—	F	Left	12.00	—	—	—
Jefferson	1928	49	M	Left	8.13	3.75	109.00	—
Carson	1930	18	M	Left	11.00	—	50.00	—
				(2 stones)	7.00	—	—	—
Cathcart	1930	48	M	Right	19.00	—	90.00	18
Patch	1930	35	M	Left	4.10	11.00	31.10	—
Grossman	1931	61	F	Right	7.50	4.50	113.00	6+
Goldman	1932	17	M	Left	18.00	9.00	125.00	—
Freshman	1932	31	M	Left	7.60	3.10	25.80	6
Taylor	1934	29	F	Left	21.50	—	45.00	6
Woodman	1934	14	M	Left	17.50	—	—	—
Muschat & Kaplan	1937	40	F	Left	5.80	5.25	43.20	1
Mayers	1940	25	M	Right	11.00	8.00	286.00	15
McKay & Baird	1947	3	M	Right	8.00	4.50	—	—
Burkland	1951	53	F	Right	16.00	4.50	24.50	32

COMMENT

In surveying the literature one does not find many instances of giant ureteral calculi, but in those presented the history is usually of long standing and most of the stones have been on the left side (see table 1). An exception is the case presented by McKay and Baird of a giant ureteral stone (8 cm. long) in a 3 year old male child. When the description giant should be applied to these calculi is usually a matter determined by personal opinion. In table 1 we arbitrarily chose a calculus measuring 5 centimeters or more in length or circumference as the definition of a giant ureteral calculus. Mayer's case is the largest reported ureteral calculus (weighing 286 gm.) and was successfully removed surgically from one of a pair of ureters representing complete duplication of the right ureter and kidney. Both of the right ureters as well as the left were greatly dilated. Taylor's patient presented bilateral bifuraction of the ureters and a large, left ureterocoele which was completely filled with a portion of the long cylindrical calculus which extended into one arm of the divided ureter. Taylor stated this was the first time such an association of a stone and congenital anomaly had been reported in the literature. It has been pointed out by Muschat and Kaplan that there are generally two types of large ureteral calculi: 1) those formed from inspissated pus and originating in the ureter proper and 2) those originally renal in origin but which become enlarged after descent into the ureter from further deposition of salts thus forming laminated calculi. The stone in our case is representative of the second type. The deposition of salts upon calculus arrested in the lower ureter causes it to enlarge in all diameters, particularly in the longitudinal, and as it grows upward it often forms a cast of the ureter.

These large ureteral calculi sometimes cause no symptoms for a long time and even if there are symptoms, they do not necessarily suggest the urinary tract. Many of the patients had vague abdominal pain or gastrointestinal manifestations for several years and it was not until frank lumbar pain, fever, and/or pyuria developed that the diagnosis was considered. With increased emphasis on the early diagnosis and the proper treatment of urinary tract infections, obstructions and calculi, giant ureteral calculi will probably not be seen very frequently in the future. In a few cases ureterolithotomy was performed with good results as in the cases of McKay and Baird, Goldman, and Mayers. In most of the cases, however, the kidney above the stone was either functionless or the seat of a marked pyonephrosis necessitating nephro-ureterectomy.

The fasting blood calcium, phosphorous and alkaline phosphatase in our patient were normal as they were in all the cases in the literature where these studies were reported. Where analyses were reported, the composition of the stones was usually mixed phosphates with occasionally calcium carbonate, oxalate and uric acid in small amounts.

Our case is the first presented where fracture of the calculus occurred in the living patient. The squamous metaplasia found in the lower end of the ureter is also of interest as a change probably due to chronic irritation from the stone. It may be analogous to the situation in the renal pelvis where squamous cell carcinoma is said to follow not infrequently the presence of a calculus in the pelvis of the kidney.

SUMMARY

A case of a giant ureteral calculus which fractured in its mid-portion in a 53 year old woman is described. A table describing the salient features of giant ureteral stones reported in the literature is also presented.

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A NEW CATHETER FOR POSTOPERATIVE URETERAL SPLINTING

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The purpose of this article is to outline the methods of ureteral splinting followed at the Long Island College Hospital, and to present a new catheter for postoperative ureteral splinting.

The frequent need for ureteral splinting after renal and ureteral surgery has been outlined by Guttierez, Gibson, Foulds and others. Today, ureteral splinting is axiomatic, and is taken for granted by most urologists.

Following most ureteral surgery involving ureterotomy, it is our custom to test the patency of the ureter with a catheter that is then left in place as a splint. Before closing the incision in the ureter, we take a conventional ureteral catheter and pass the rounded end first up and then down the ureter to assure the patency of the lumen. After this, the rounded end is again passed up to the kidney pelvis and made to drain. The distance to the pelvis is then noted by the markings on the catheter. The other nonrounded, or "square" end is passed down the ureter into the bladder. By an easy maneuver the catheter is left in situ, and its position readily checked by observing the markings which were previously noted. The ureterotomy is closed with 4-0 chromic atraumatic catgut, a small Penrose drain is left into the site of ureterotomy about thirty-six hours. The splinting catheter has served its purpose in a week, and is removed cystoscopically at that time. Failure of drainage of the splinting catheter is indicated by pain and elevation of temperature. Should this occur, the catheter is brought out through the external meatus, and by irrigation made to drain properly. Here, too, the catheter is removed after a week.

Two problems arose with this method: 1) The square end of the catheter either traumatized the distal ureter as it passed down or could not be passed at all; 2) in the bladder, it was often difficult to recognize the distal end of the catheter. Often a loop of catheter would be grasped with the cystoscopic rongeur, and a large portion of the catheter displaced from the ureter. Even a slight downward displacement would pull the catheter out of the kidney pelvis so that it could not be irrigated. Either would nullify the purpose of the catheter so that the identification of the tip of the catheter and its careful removal from the bladder became imperative. To obviate these difficulties, with the help of C. R. Bard, Inc. of Summit, N. J., and Mr. James A. Vassar, a two-ended catheter was made. This catheter consists of standard materials, 70 cm. long, and made in 7, 8 and 9F. It is rounded at both ends, with double eyes. The catheter is marked toward the center from both ends. The terminal centimeter at both ends is brightly colored. These innovations permit ready passage up and down the ureter, and assure identification of the end of the catheter, eliminating the difficulties outlined (fig. 1).

The catheter is irrigated by passing a size 20 needle on a syringe into the proxi-

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mal eye, and occluding both eyes with the thumb and forefinger. The catheter is attached to drainage tubing by passing it through a nipple on a glass connecting piece.

The catheter and method have the following advantages: 1) easy passage up and down the ureter by way of the ureterotomy; 2) ready identification of the distal tip cystoscopically; 3) primary closure of the ureterotomy with adequate splinting; 4) elimination of use of T-tube, pyelostomy, or nephrostomy with drainage, and possible fistula formation; 5) elimination of possible perforation of ureterotomy wound with a catheter passed postoperatively; 6) decreased possibility of infection or pain; 7) multiple catheters may be used, as suggested by Gibson.

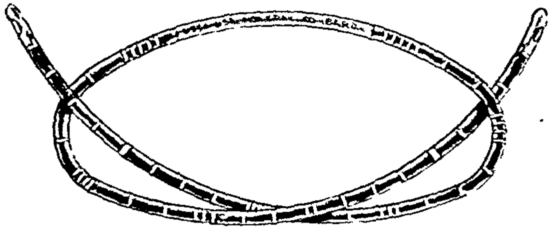

FIG. 1. Halftone drawing of catheter

The only disadvantage is the necessity for cystoscopic removal.

This catheter has been used in 4 cases of lower ureteral calculus. The results were excellent clinically, and it lived up to our expectations mechanically and technically. We recommend its use in ureterolithotomy, stricture and other plastic repairs necessitated by trauma, infection, fistula or neoplasm. We do not doubt that in the future we will find other uses for this innovation.

SUMMARY

The need for ureteral splinting has been reaffirmed.

The technique of in situ ureteral splinting with primary closure of the ureter (elimination of T-tube, pyelostomy or nephrostomy), has been outlined.

A useful new catheter is offered to simplify postoperative ureteral splinting.

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PERICYSTITIS

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Pericystitis is an inflammation of the cellular tissues around the urinary bladder. It may lead to cellulitis or to suppuration, and it may follow inflammation of the bladder itself, or spread to it from adjacent tissues or organs. This condition can be primarily bacterial in origin, or it may take the form of an aseptic process as a complication of a degenerating neoplasm or of a mechanical trauma. Campbell has described a variety which follows removal of the rectum and produces a rigid bladder which cannot empty completely, but which does not lead to pyuria. The literature on pericystitis has been reviewed thoroughly by Winsbury-White and by Goldstein and Abeshouse, and will not be discussed further in this brief communication, the purpose of which is merely to call attention to an unusual case of pericystitis due to osteomyelitis of the ischium.

CASE REPORT

C. R. H., a well developed and nourished white man of 32, was admitted to St. John's Hospital in Fargo, North Dakota on August 12, 1947, complaining of recurrent pyuria of 1 year's duration. He had had an acute osteomyelitis of the right ischium in 1942. A contracture of the vesical neck had been resected by the writer in March 1947.

On admission the temperature was 101.4F and the pulse 100. The morphology and urea nitrogen of the blood were normal. Urinalysis showed albuminuria grade 3 as well as 10 to 15 red and 15 to 20 white blood cells per high powered field. Definite tenderness without muscle spasm was present in the right lower quadrant of the abdomen. Rectal examination disclosed a smooth, firm, slightly tender mass above and to the right of the prostate gland.

Cystoscopic examination revealed a diffuse bullous edema of the right wall of the bladder with conspicuous reddening of the mucosa. Divided specimens of urine were free from pus and sterile on culture. Retrograde pyelograms were normal, but there was evidence in the roentgenogram of chronic osteomyelitis of the right ischium with sequestration (fig. 1).

The patient was seen in consultation at St. Barnabas Hospital in Minneapolis by C. D. Creevy, M.D. on September 13, 1947. The findings at cystoscopy were identical with those just described. Biopsy of the inflamed vesical mucosa showed only subacute inflammation. The diagnosis of cystitis secondary to extension from osteomyelitis of the right ischium was confirmed, and removal of the affected ischium with drainage of the abscess were recommended.

The involved ischium was removed at St. John's Hospital in Fargo in collaboration with Dr. Joel Swanson, orthopedic surgeon, on September 18, 1947. The pathological report was as follows: "The gross specimen consists of three fragments of softened bone. Microscopic: There is considerable destruction of bone

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with sequestration. In some areas the bone has lost its normal characteristics and appears to be undergoing absorption. Osteoclastic activity in these areas is intense. In other areas new dense bone is being laid down. A minimum of polymorphonuclear infiltration is present. Diagnosis: Chronic osteomyelitis. J. D. LeMar, pathologist."

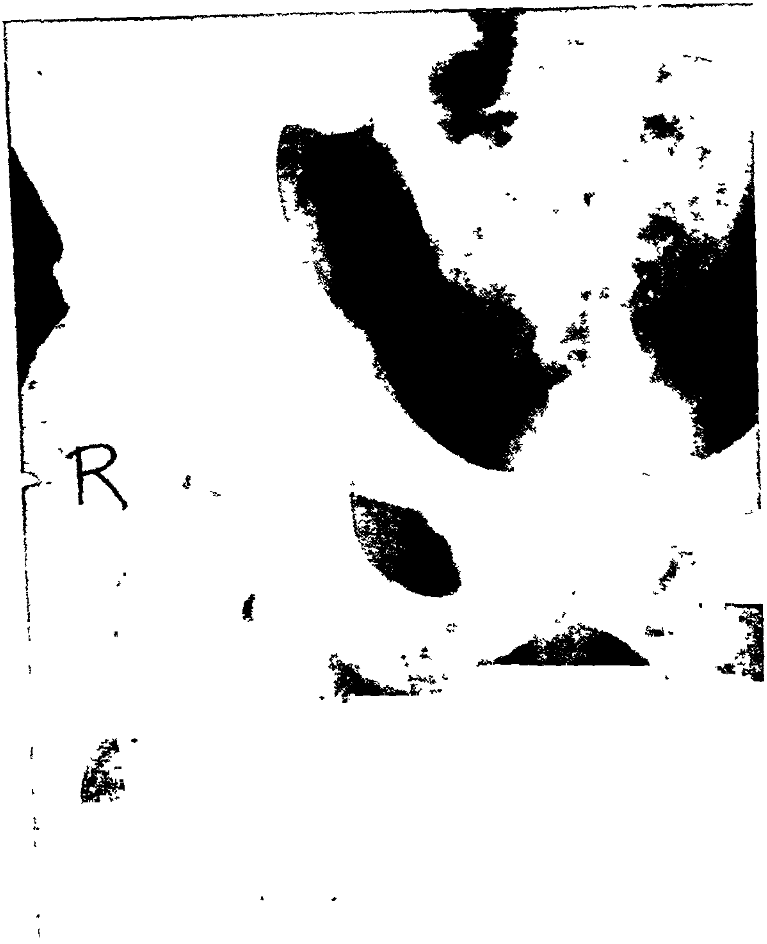

FIG. 1. Osteomyelitis of right ischium

By the tenth postoperative day it was evident that the perivesical abscess was not draining adequately through the perineum. It was therefore evacuated through a median suprapubic incision, a Penrose drain being left in place. Staphylococcus aureus was cultured from the pus. Antibiotics were administered and both wounds healed rapidly. The patient was discharged from the hospital one week after the second operation. The abdominal discomfort had disappeared and the urine was normal. He has remained perfectly well for the past five years.

He has declined to submit to cystoscopic examination, but the urine has remained normal, as was an excretory urogram in March 1951.

SUMMARY

A case of chronic purulent pericystitis (perivesical abscess) secondary to chronic osteomyelitis of the ischium is presented.

Since five years have elapsed since operation, it seems reasonable to assume that the patient is cured.

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A CLINICAL AND PATHOLOGICAL STUDY OF CARCINOMA OF THE URINARY BLADDER

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The proper evaluation of carcinoma of the urinary bladder from the standpoint of therapy and prognosis is difficult, and in spite of extensive clinical studies, is not decisively settled. Although of value in diagnosis and histological grading, many surgical specimens do not give the answer to the significant problem of degree of penetration and spread. Ash concluded that a satisfactory system of grading tumors, particularly the papillary ones, was very difficult to devise because of the great variance between the clinical course and histologic picture. He stated that the most practical method of grading was based on a combination of physical findings and the histo-pathological examination. Graves, Buddington and Thomson found that biopsy reports provided confirmatory evidence for the clinical diagnosis of cancer, but presented no close agreement with the grade of malignancy as determined by the pathologists from the final specimen. Berry and Hamilton reported that a biopsy obtained by the resectoscope, properly taken and correctly prepared, gave accurate information on bladder tumors and compared favorably with those taken at operation. Jewett stated the incidence of extravesical spread was directly proportional to the depth to which the tumor had penetrated the bladder wall. The clinical determination of the depth of penetration of the bladder wall may provide the index of potential curability. Kerr and Colby believed that the actual microscopic evidence of muscle invasion was significant and considered that clinical impressions were considered inaccurate. Yet, in the postoperative specimens of 700 cases of carcinoma of the bladder, they found only 135 tumors with adequate sections and follow-up for study.

THE PRESENT STUDY

In an attempt to correlate clinical grading, histological classification, and microscopic grading of bladder tumors with treatment and prognosis, 96 consecutive cases of malignant neoplasms of the urinary bladder treated at John Sealy Hospital from 1940 to 1950 have been analyzed. These cases were consecutive and not selected, for it is believed that if the grading is to have any practical significance it must be applicable to almost every case of bladder tumor, and not only when the entire thickness of the bladder wall is submitted for study.

Since the clinical grading was used as the primary guide for treatment and prognosis, the tumors were divided into four categories according to the clinical estimation of the depth of penetration of the bladder wall. This was then compared to the actual microscopic determination of muscle invasion and to the histological grading. The clinical and microscopic invasiveness of a neoplasm were thus based largely on Jewett's method of classification of bladder tumors. Grade

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1 tumors were those which were confined to the mucosa and submucosa of the bladder with no evidence of muscle infiltration. Clinically, this was determined by the gross appearance of the tumor and its pedicle, the character of the bladder wall about the tumor, biopsy specimens when helpful, and bimanual examination under anesthesia. Included in the grade 2 tumors were those which gave evidence of early invasion of the muscular wall or, if it was possible to estimate, involved less than one-half of the width of the bladder wall. Grade 3 tumors were those which were estimated to involve more than one-half of the depth of the musculature, but which were still confined to the bladder wall. The tumors that had extended beyond the bladder wall and into the perivesical tissue or had metastasized were considered inoperable except for palliation and were classified as clinically grade 4 tumors.

The operative specimens in each case were examined microscopically and classified according to depth of penetration of the bladder wall. The microscopic invasion of specimens was graded as A, B, C, and D with the criteria similar to the clinical classification of 1, 2, 3, and 4. The histological grading of the neoplasm was based on the cellular anaplasia according to the classification of Broder. Grade 1 represented a neoplasm composed of uniform cells with infrequent mitoses and absence of invasion. In grade 2 tumors, the cells were thrown into sheets that varied from 7 to 16 layers. An occasional mitotic figure was noted in this group. Grade 3 or 4 represented more anaplastic lesions, with grade 4 being the most undifferentiated. The histological classification was based on the histogenesis of the neoplasm. Table 1 presents a general summary of the clinical classes and their respective grading according to microscopic muscle invasion, and histological grading.

TABLE 1. *Distribution of malignant neoplasms of urinary bladder according to microscopic grade and invasion**

CLINICAL GRADE	MICROSCOPIC GRADE				EXTENT OF INVASION					
	1	2	3	4	O	A	B	C	D	⨳
I (17)	12	4	1	0	8	8	1	0	0	0
II (34)	11	14	7	2	16	5	6	3	1	3
III (26)	3	7	12	4	3	3	4	6	6	4
IV (19)	1	3	11	4	8	1	0	1	5	4

* Invasion indicated as follows: O—Unable to determine invasion in tissue submitted for microscopic study. ⨳—Invasion of muscle present but depth could not be determined A—Submucosal infiltration. B—One-half of muscularis. C—Greater than one-half of muscularis but still confined to bladder wall D—Perivesical infiltration.

Due to the variability of behavior of bladder tumors, classification of postoperative results was very difficult unless the patient was followed until death, and post-mortem examination with adequate microscopic examination done. Even, then, the effect of the tumor on the general health could not be determined with absolute certainty in every case. Postoperative results were therefore classified as satisfactory, unsatisfactory, and questionable. The satisfactory cases were those who at the time of evaluation or death were free of tumor as far as could be determined. The unsatisfactory cases were those who were living with uncontrolled cancer, or those who had died with cancer, whether or not it had contributed to their death. The questionable cases were those in whom it was impossible to determine whether tumor was present at the time of study or at the time of death. To be classified as satisfactory, the patient had to be followed for at least 1 year; otherwise, the case was classified as questionable. It is realized that the follow-up interval in many of these cases was not sufficient. Many of the patients died at home, and no post-mortem could be obtained. To help in evaluating postoperative results, the Commissioner's Standard Ordinary Mortality Table was used to compare the actual survival time of the patients with their average life expectancy when first treated.

Age, race, sex, symptoms and complications. The average age in these cases was 62 years, the youngest patient being 34, the oldest 89. Eighty were white and 16 colored. There were 77 males and 19 females; a ratio of approximately 4 to 1.

Gross hematuria was a prominent symptom in 80 patients, burning on urination in 40, frequency in 27, nocturia in 25, urgency in 12, difficulty in initiating urination in 7 and suprapubic pain in 5. The average duration of symptoms prior to treatment was 12 months; the shortest being 3 days and the longest 5 years. Forty-three of the cases (44 per cent) showed some degree of urinary tract infection. Fifty per cent had other complications that had to be considered in contemplating a formidable procedure. These complications were largely organic heart disease on an arteriosclerotic or hypertensive basis. Upper urinary tract disease was not included unless of a serious nature.

CLINICALLY GRADE 1 TUMORS

Microscopic muscle invasion. In the seventeen clinically grade 1 tumors, there was very little discrepancy in the three classifications. A summary of each case is given in table 2. In 8 cases (47 per cent), it was impossible to tell by study of the postoperative specimens, whether or not the muscle was involved. In eight other cases, there was no invasion of the musculature. In only one instance (case 1) did the microscopic sections show muscle invasion, and this tumor was also a histological grade 2. At his original admission this patient was 73 years of age, and he lived 9 years with cause of death unknown. Since, by the Commissioner's 1941 Standard Ordinary Mortality Table. his life expectancy was 7.6 years, this can be classed as a fairly satisfactory response. However, he had seven recurrences during this time, and 6 years after the original admission, the new growths became more malignant clinically, necessitating a partial resection of the bladder. Deming reported, in his series of 109 cases, that 7.3 per cent of transitional cell papillomas became more malignant as the patients were followed.

Microscopic grading and classification. Twelve of the 17 patients with clinically grade 1 tumors were also classified as histological grade 1, and of these, only one was seen with one or more recurrences. Four of these seventeen tumors were histologically grade 2 and interestingly all four of these patients had one or more recurrences. Only 1 case (No. 17) was classified as a histological grade 3. It was unfortunate that this occurred in a patient 89 years old with severe arterioscle-

TABLE 2. *Malignant neoplasms of urinary bladder, 96 cases*

CASE NUMBER*	HISTOLOGICAL GRADE	EXTENT OF INVASION†	SURVIVAL IN YEARS‡	LIFE EXPECTANCY, YEARS§
Clinical Grade I				
1	II	B	9	7.6
2	I	A	1	
3	I	O	2	
4	II	O	3	
5	I	A	2	
6	II	A	17	21.3
7	I	A	2	
8	I	A	2	
9	I	O	3	
10	I	O	2	
11	I	O	1.5	9.4
12	I	A	Lost	
13	II	O	3	
14	I	A	4	
15	I	O	6	
16	I	A	2	
17	III	O	1	2.7
Clinical Grade II				
18	I	O	3	
19	I	O	12	
20	I	A	3	
21	III	C	⅔	
22	II	O	15	
23-S	III	B	1½	12.7
24	III	C	½	
25	II	O	1	
26	IV	#	5	11.
27	III	B	2	14.5
28-S	II	C	2	
29	I	O	3	
30	II	A	1½	
31	I	O	6	
32	II	O	6½	9.9
33	III	B	3	
34	II	O	4	
35	I	B	2	
36	II	O	7	
37	II	O	1	
38	II	O	10	
39	I	O	3	
40	II	O	Lost	
41	I	A	5.5	8.9
42	I	O	4	
43	II	B	4	
44	III	#	13	14.5
45	IV	D	½	8.9
46	II	O	4	18.4
47	II	#	2	
48	I	O	3	10.5
49-S	II	B	1/12	8.0
50	I	A	5	
51	III	A	1	8.5
Clinical Grade III				
52-S	III	D	0	21.3
53	II	B	¼	7.6
54	III	C	0	23.6
55	III	O	1	14.5
56	I	A	⅙	3.9
57	III	#	½	21.3
58	III	C	1	
59-L	IV	#	⅓	4.7
60	IV	D	1/12	13.2
61	III	C	1	23.6
62	I	A	2	
63	III	C	1	12.1
64	III	D	0	12.6
65	I	O	1/12	
66	II	O	2	
67	III	#	7	
68	IV	D	Lost	
69	III	C	¼	13.8
70-S	II	D	1	20.6
71-S	IV	B	1	
72	III	D	6	
73	II	B	6	
74-A	II	C	⅔	23.6
75	II	B	3	8.5
76	II	A	4	11.5
77	III	#	2	17.1
Clinical Grade IV				
78	III	D	¼	30.0
79	III	#	¼	14.5
80-S	III	O	⅓	8.5
81	IV	D	0	8.5
82	II	O	⅔	8.9
83-S	III	O	Lost	
84	II	#	¼	26.8
85	II	O	¾	11.5
86	I	A	1	
87	III	#	¼	15.7
88	IV	O	1/12	8.9
89	III	D	0	17.7
90	III	C	⅙	15.1
91	III	D	0	8.5
92-S	IV	D	0	15.1
93-A	IV	O	⅙	9.9
94	III	O	0	5.0
95-S	III	O	⅙	30.9
96	III	#	⅔	4.7

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* Diagnosed as Transitional Cell or -S—Squamous Cell; -A—Adenocarcinoma; -L—Leiomyosarcoma.

† As defined in Chart I.

‡ Sruvival from date of treatment.

§ From Commissioners 1941 Standard Ordinary Mortality Table. For cases that have expired.

rotic heart disease. He died 1 year later, apparently of arteriosclerotic heart disease; no autopsy being performed. However, during this interval, he returned twice with multiple recurrences, clinically grade 1 in type. His life expectancy at the beginning of treatment according to the Commissioner's 1941 Standard Ordinary Mortality Table was 2.7 years. All of these clinical grade 1 neoplasms were classified as transitional cell carcinoma.

Only 1 case (No. 6) could be classified as unsatisfactory in response. This patient died 17 years after initial treatment, at the age of 50. His life expectancy at the time of diagnosis had been 21 years; thus, he had almost completed the anticipated survival time comfortably. Shortly before death he was found to have an inoperable tumor of the right ureter although his bladder was free of growth. Histologically the bladder tumor was grade 2. It is felt that clinically grade 1 tumores with a histological grade of 2 or greater offer a distinctly graver prognosis than those which are histologically grade 1.

Results. Of the 17 cases, ten were confined to the lateral walls, six to the trigone, and one to the bladder neck. There was no apparent relationship between the location and the degree of malignancy. Eight patients had multiple tumors originally and in four instances, there were recurrences. However, in two patients with seven or more recurrences, the original tumor was single.

Twelve patients are known to be living for an average of 3.6 years, and four are dead surviving for an average of 7.1 years. Fourteen cases were considered satisfactory and free of tumor, one was unsatisfactory, having died of tumor of the ureter, and two cases were questionable. One of the questionable cases could not be followed. The other (No. 11) died 1.5 years after treatment, 7.9 years short of his expected survival. The cause of death was given as cardiac failure. In all instances, with these questionable exceptions, the patients had comfortably completed practically all their life expectancy.

CLINICALLY GRADE 2 TUMORS

Microscopic muscle invasion. Of the 34 clinically grade 2 tumors, in 16 cases (47 per cent), it was impossible to determine whether the muscle was invaded. Twelve (73 per cent) of the 16 cases are living and considered to have been successfully treated, having been followed for an average of 5.8 years. One of the sixteen (No. 32), with a life expectancy of 9.9 years, died of the effects of his tumor 6.5 years after initial treatment. Three cases were questionable, two having died suddenly with no evidence of metastases clinically. One (No. 46) lived 4 years with a life expectancy of 18.7 years, and the other (No. 48) 3 years with an expectancy of 10.5 years. One patient could not be followed.

In the microscopic sections of three patients (8.8 per cent), muscle invasion could be seen, but the depth could not be determined. Two cases were considered satisfactory; one is living without incident two years after operation, and the other, with a life expectancy of 14.5 years, died 13 years after operation without evidence of recurrence. The unsuccessful case, with a expected average survival of 11 years, died five years after treatment of widespread metastases. The microscopic sections of 5 patients (14.7 per cent) revealed grade A invasion. Four of these were thought to have been successfully treated after having been followed for an average of 3.7 years. One patient (No. 41), with an expected survial of 8.9 years, died after 5.5 years of generalized tuberculosis. The others are living and well at 1.5, 3 and 5 years. One questionable case (No. 51), with a life expectancy of 8.5 years, died 1 year after treatment, the cause of death clinically being bronchopneumonia.

In 6 instances (17.7 per cent), the patients were found to have grade B infiltration of the musculature. Only three (50 per cent) of these were considered satisfactorily treated, having been followed for an average of 3 years. One patient died of pulmonary metastases after 2 years although the life expectancy had been 14.5 years. Two cases were questionable since both died suddenly without evidence of tumor clinically. However, one died after 18 months with a life expectancy of 15.7 years and the other after one month, with an expected survival of 8 years. Thus, it is very likely that these two cases were actually unsuccessful and died of the effects of the bladder tumors.

Three of the cases (8.8 per cent) showed grade C invasion of the musculature. One was considered successful although he had been followed for only two years. In one patient pelvic metastases developed 9 months after operation. The remaining patient is living without recurrence, but has been followed for only 7 months.

In the sections of only 1 patient in this series was grade D invasion of the bladder wall found. As expected, he lived for only 6 months with an anticipated average expectancy of 8.8 years.

Microscopic grading and classification. Eleven cases (32 per cent) of the 34 clinically grade 2 tumors were classified as histological grade 1. It is interesting to note that 10 patients have done well, being followed for an average of 4.6 years. One questionable case died suddenly after 3 years with no demonstrable metastases on follow-up.

Fourteen cases (41 per cent) were designated as histological grade 2 and in the group there were two squamous cell carcinomas. Ten (72 per cent) of these 14 cases were considered to have received therapy satisfactorily, having been followed for an average of 4.9 years. Only one case was definitely unsuccessful, and three were questionable. It would seem that a clinically grade 2 tumor with a histological grade of 2 should give a fairly satisfactory prognosis.

Seven (20 per cent) of the tumors were histological grade 3, one of which was squamous cell carcinoma. Only two (38 per cent) of the 7 cases in this group have done well after being followed for an average of 8 years. Two were unsuccessful, one living with pelvic metastases, and one having died of pulmonary metastases. The three cases designated as questionable are suspected of being actually unsatisfactory.

Only 2 cases were classified as histological grade 4, and both had widespread metastases demonstrated either at operation or autopsy. Apparently a grade 2 tumor clinically with a histological grading of 3 or 4 offers a more serious prognosis than a histological grading of 1 or 2.

Results. In this series of 34 cases, twenty-two (64 per cent) were satisfactory, five (14 per cent) unsuccessful and seven (22 per cent) were questionable. The 11 patients who have died failed to reach their life expectancy by an average of 7.9 years. Seventeen tumors originated from the lateral walls, eight from the trigone, three in the vault, five about the bladder neck and one on the posterior wall. Fourteen of the tumors were multiple, and in eight of these there were one or more recurrences. Of the twenty single tumors, there were ten with recurrences. Five (45 per cent) of the tumors of this group with a histological grade 1 recurred. The average recurrence for the entire group was 52 per cent. Three cases were classified as squamous cell carcinomas and 31 were transitional cell carcinomas. A brief summary of each case is given in table 2.

CLINICALLY GRADE 3 TUMORS

Microscopic muscle invasion. Of the 26 patients with clinically grade 3 tumors, in only three (12 per cent) was it impossible to determine if muscle invasion had occurred. One was considered successful; however, he had been followed for only 2 years after operation. One patient had been followed for only 7 months without incident and was designated as questionable. The other case (No. 55) was unsuccessful since the patient died of widespread metastases 1 year after operation.

Three (12 per cent) in the series showed no invasion of the musculature microscopically. One patient has done well for 2 years after operation. It was unfortunate that 1 patient (No. 56) died in an automobile accident 2 months after operation and was considered questionable. The other patient (No. 76) was also questionable; he died suddenly 4 years after operation without tumor clinically, but his life expectancy was 11.5 years.

There were 4 cases (15 per cent) which showed muscle invasion, but the depth was impossible to determine. One patient has lived for 7 years without recurrence. Two cases were definitely unsuccessful with demonstrable metastases. One patient (No. 77) was considered questionable having died suddenly without demonstrable metastases fifteen years short of his expected life span.

The microscopic sections of 4 patients (15 per cent) revealed grade B invasion of the bladder wall. One patient has done well and is living 6 years after operation without incidence. The other 3 cases were unsuccessful. One is living 1 year after operation with widespread metastases. One died of the effects of the bladder tumor after 3 months, and the other 3 years following treatment.

Six cases (23 per cent) had grade C invasion of the musculature. One patient (No. 58) was considered satisfactory although he had been followed for only 1 year after total cystectomy. Four patients have died of tumor, having lived for an average of 20.7 years short of their expected life. The questionable case lived only 1 year after operation, with an expected survival of 12 years.

Six patients presented grade D extension into the bladder wall microscopically. One patient has done well for 6 years following treatment. Four patients died of the effects of their bladder tumor, having survived for an average of 16.6 years short of their expected life. One patient could not be followed.

Histological classification and grading. Three of the tumors were classified as histological grade 1. One is living without incident 2 years after operation. Two are living, but questionable since they have been followed for less than 1 year.

Seven were histological grade 2 tumors. Two have done well and four were unsuccessful. Of the four unsuccessful cases, one was a squamous cell carcinoma and another an adenocarcinoma. One patient died suddenly without clinical evidence of metastases.

Histological grading of 12 tumors was grade 3, one of which was classified as a squamous cell carcinoma. Three were satisfactory, seven unsatisfactory and two questionable. Four were grade 4 tumors, one being a squamous cell carcinoma and the other being leiomyosarcoma. Three were unsuccessful and one could not be followed.

Results. Of the 26 cases of clinically grade 3 tumors, six (23 per cent) were considered satisfactory, fifteen (58 per cent) unsatisfactory and five (19 per cent) questionable. Seventeen patients have died, and they failed to reach their life expectancy by an average of 14.1 years. Only five of the grade 3 tumors were multiple, and of these five, two recurred. Six tumors apparently originated from the trigone, two from the bladder neck, six from the lateral walls, three from the posterior wall and three in the vault. In 6 cases, the tumor was so extensive that it was impossible to determine the site of origin. The cases in this group are summarized in table 2.

CLINICALLY GRADE 4 TUMORS

Microscopic muscle invasion. All 19 cases of clinically grade 4 carcinoma of the bladder, as expected, were unsuccessful. Only one is known to be living and one could not be followed. In 8 patients, it was impossible to tell whether muscle was invaded by microscopic sections. However, some of the patients were terminal and inadequate biopsies were taken to determine the invasion of the neoplasm. One patient showed no invasion of the musculature in postoperative specimens. However, this case was included in the grade 4 category because of an inoperable tumor of the right ureter and not on the appearance of the bladder lesion. Histological grading of this tumor was also grade 1. In 4 cases (21 per cent) it was possible to determine muscle invasion, but impossible to estimate depth. No tumors in this group were grade B by invasion, and there was only one grade C. Five cases (26 per cent) were grade D by microscopic sections.

Microscopic classification and grading. Three of the cases were histologically grade 2, eleven patients were grade 3, of which three were squamous cell carcinomas, and four were grade 4, of which one was a squamous cell carcinoma. No histological grade 1 carcinomas were included in this group except the 1 case mentioned previously.

Results. Of the 17 patients known to be dead, their survival was on the average 14 years short of their expected life span. In practically every case, it was impossible to determine the exact site of origin or multiplicity because of the extensiveness of the tumor. A summary of each case is presented in table 2.

TREATMENT

Clinically grade 1 tumors. Therapy of the clinically grade 1 tumors was entirely by transurethral resection and fulguration except in 1 patient in whom a partial cystectomy was necessary 6 years later. Since other recurrences were superficial in nature, they were treated by repeated endoscopic procedures. Thomas believes that radical surgery is immediately indicated if there are local recurrences subsequent to transurethral resection. It is felt that the results in this series could be considered successful since the patients who have died had almost completed their life expectancy comfortably. The single unsatisfactory case had almost lived to this expectation without discomfort. It would seem that more formidable operations in this group would have added increased operative risks and discomfort without adding appreciably to the survival time. In a series of 100 cases of total cystectomy by Marshall and Whitmore, there were 40 cases of cancer extending just to the muscle. Of these, there were only 26 successful 2-year survivals, and out of this twenty-six, seventeen had only superficial lesions. It might be significant that no patient developed as many as ten tumors per year in this group. Deming states that for those cases which develop more than ten tumors per year, a total cystectomy is advocated. Kerr and Colby are of the opinion that tumors not invading the muscle should be treated by methods other than cystectomy, if possible. Our results would confirm this conclusion.

Clinically grade 2 tumors. Of the 34 clinically grade 2 carcinomas, 20 were treated by transurethral resection and fulgurization; of these, thirteen (65 per cent) were considered satisfactory having been followed for an average of 4.7 years. There was one 15 year follow-up, one over 10 years, two more than 5 years, and the remainder have been followed less than 5 years. In 8 of these 13 satisfactory cases (61 per cent), it was impossible microscopically to estimate the depth of infiltration. Microscopically one showed grade A invasion, two grade B, and in 2 cases the depth of invasion could not be estimated. Histologically four of these thirteen successful cases were grade 1, eight were grade 2 and one grade 3. Three (15 per cent) of the 20 patients treated by transurethral resection were definitely unsuccessful. In one instance, it was impossible to determine microscopically if muscle invasion had occurred. One revealed grade B invasion, and one grade D invasion. By histological grading, one was grade 2, one was grade 3 and the other grade 4. The remaining four, although considered questionable, of course, were potentially unsatisfactory.

Of the 5 patients treated by suprapubic cystotomy and electrocoagulation all are living and considered successful, having been controlled for an average of 6.8 years. Two patients have been followed for over 10 years, one for over 5 years, and two less than 5 years. Microscopic sections of two showed only grade A invasion of the bladder wall, and in three it was impossible to tell if muscle had been infiltrated. It might have been significant that by microscopic grading, three were grade 1 and two were grade 2.

Of 9 patients treated by partial cystectomy, only 4 (44 per cent) were considered successful. However, these four have been followed for only an average of 3.2 years. Microscopically one revealed grade A invasion, one grade B invasion, one grade C invasion, and in the fourth, it was impossible to tell if muscle infiltration had occurred. Two were grade 1 transitional cell carcinomas, one was a grade 2 squamous cell carcinoma, and one was a grade 3 transitional cell carcinoma. In two, extensive metastases have since developed. In the sections of 1 case, muscle was invaded but the depth could not be determined; the other showed grade C invasion. The histological grading of one was grade 3, the other grade 4. Three cases were considered questionable.

The most satisfactory therapeutic results in this group of clinically grade 2 carcinomas were obtained by suprapubic cystotomy and electrocoagulation. However, it is interesting to note that 2 patients had only grade 1 invasion microscopically and by histological grading, three were grade 1 and two were grade 2. Thus, although the tumors were clinically grade 2, their biological behavior was probably less malignant than the majority of the other grade 2 tumors. Although only 15 per cent of the cases treated by endoscopic procedures were definitely unsuccessful, it must be realized that 20 per cent were questionable, and the patients could very easily have died of the effects of their bladder tumors. Muscle invasion in these could not be determined in a sufficient number of cases to be informative. It might be significant in the successful cases that by microscopic grading only one was grade 3, the remaining tumors being less anaplastic. It is believed that transurethral resection is a fairly successful method of treating grade 2 tumors, and certainly involves the least amount of operative risks in the elderly patient. In many instances, the tumor surrounded one of the urethral orifices of the bladder, and of necessity, these tumors were resected deep into the musculature. No ill effects were noted in any of the patients postoperatively. Higgins stated that in his series complete excision of the tumor, without injury to the ureters or vesical sphincter which may result in incontinence, was impossible in 72.5 per cent. It is surprising that only 44 per cent of the cases in this group treated by partial cystectomy have done well. It is the procedure, short of total cystectomy, which would be expected to give the greatest possibility of cure. It is possible that the examiner, through experience, regarded this group as potentially more malignant than the remainder, and thus advocated partial cystectomy rather than a more conservature procedure. The role of total cystectomy in clinically grade 2 tumors is questionable. Kerr and Colby found when all forms of treatment were used, in tumors that involved the muscle, the end result was essentially the same whether or not cystectomy was performed. In this series, total cystectomy was not performed in clinically grade 2 tumors, and overall reports from other clinics have not been encouraging enough to alter this procedure.

Clinically grade 3 tumors. Five of the 26 clinically grade 3 tumors were treated by transurethral resection and fulguration. Of the five, only two were satisfactory, one having been followed for 7 years, and the other for only 2 years. In one of these, although muscle was invaded, the depth could not be determined; and in the other, muscle invasion could not be determined. One was a microscopic grade 2 and the other a microscopic grade 3. One case which was definitely unsatisfactory revealed grade B muscle invasion with a microscopic grade 2. Although 2 cases were questionable, they very likely died of the effects of their tumors. Only one of the 6 patients treated by suprapubic cystotomy and electrocoagulation of the lesions was successful, having been followed for only 1 year. It is interesting that this tumor presented grade A invasion and a microscopic grade 1. Of the three unsuccessful cases, one showed grade B muscle invasion and grade 2 microscopic, and in two there was muscle invasion with the depth undetermined and grade 3 microscopic. Two were questionable.

Nine patients of this group were treated by partial cystectomy. Only two are living without tumor, both having been followed for 6 years. In one, there was found grade B muscle invasion with microscopic grade 2. In the other, muscle invasion was grade D with a grade 3 microscopic. Six patients died with tumor. In one, there was grade D invasion with grade 3 microscopic; one grade C invasion with grade 3 microscopic; one showed muscle invasion with grade 4 leiomyosarcoma; and the other grade C invasion with a grade 2 adenocarcinoma. All of these unsatisfactory cases apparently had highly malignant tumors. One case is questionable.

Six patients were treated by total cystectomy. The treatment of only one was considered successful, and he has been followed for only a year. This tumor was classified as grade C invasion with a microscopic grade 3. Three had tumor remaining following operation. One revealed grade B invasion; however, microscopically the classification was grade 4 squamous cell carcinoma. In one, there was grade C invasion with grade 3 microscopic, and in the other there was grade D invasion with a grade 2 squamous cell carcinoma. Two patients died during their postoperative period from the effects of operation.

In the clinically grade 3 tumors, only occasional satisfactory treatment was obtained with all methods of therapy. Most of the unsatisfactory cases had highly malignant tumors. Total cystectomy certainly did not improve the prognosis of this group. The only definite indication from this series that has been found for cystectomy is a highly malignant, deeply invasive tumor of the trigone or bladder neck in the younger age groups, preferably in the fifth or sixth decade. Partial cystectomy when technically feasible would seem to give almost as good a possibility of cure. Jewett and Lewis stated that when infiltration was deep, it was so recognized by preoperative palpation and of these, there were no acceptable instances of cure by total cystectomy. Kerr and Colby found that 40 per cent of fifteen tumors that invaded muscle involved the regional lymph nodes. Leadbetter and Cooper found that 26.6 per cent of patients with deep muscle and perivesical invasion have involvement of the pelvic and common iliac lymph nodes. In this series, pelvic lymphadenectomy was carried out only occasionally. However, this is not thought to be particularly significant in the end results. Priestley believes that it appears unwise to perform cystectomy if the growth has extended beyond the bladder in such a manner that its complete removal is questionable. Kerr stated that one cannot do adequate pelvic dissection without removing the rectum which he does not believe is justified. Bandler is of the opinion that distant metastases can be produced only by means of blood vessel spread which concerns the relationship of the vertebral veins to spread of metastases.

Grade 4 tumors. Nineteen patients had clinically grade 4 tumors. No patient could be considered satisfactory regardless of the treatment attempted, which was for palliation only. For 2 patients, a total cystectomy was done as a palliative measure, and the results were questionable. According to Doroshow, 52 per cent of the cases of urinary diversion to the rectosigmoid show a blood electrolyte alteration which presents an additional chemical hazard. In two other patients, cutaneous ureterostomy was done.

Location of the tumor apparently did not affect the malignancy or prognosis of the tumors. It influenced this series only in that it made some operations technically more feasible than others.

Deep x-ray therapy was utilized only for palliation and in no case were any significant results obtained. Radium therapy was attempted in one patient with no apparent alteration of the course of his disease.

DISCUSSION

The clinical grading in combination with the histological grading of transitional cell carcinoma of the urinary bladder seemed to best reflect their subsequent behavior. Follow-up studies of the 13 cases of squamous cell carcinomas indicated a poor prognosis in this group since only 1 case has survived 2 years after treatment. The two cases of adenocarcinoma and one case of leiomyosarcoma had very short survival periods following therapy and were classified as unsatisfactory. Both of the cases of adenocarcinoma were located in the superior portion of the urinary bladder near the fundus. This location, as well as the histological appearance, would suggest that these neoplasms arise from remnants of urachus. The diagnosis of leiomyosarcoma was considered in 1 case only after a study of multiple sections. Fifty-two per cent of the neoplasms in this series were multiple tumors. Some have attributed this multiplicity to implantation metastases, and others to multifocal origin of these neoplasms.

In general, clinical grade 1 or 2 transitional cell carcinomas with well differentiated histological features have a better prognosis than the same clinical grades with microscopic grade 3 or 4 classification. The clinical grade 3 and 4 groups of neoplasm should have a guarded prognosis regardless of the histological grading of the neoplasm.

The extension of the neoplasm into the wall of the urinary bladder has been stressed by many writers as an important prognostic feature. In 47 per cent of the clinical grade 1, 47 per cent of clinical grade 2, 11.5 per cent of clinical grade 3 and 42.2 per cent of clinical grade 4, the presence of invasion could not be ascertained by examination of the tissue submitted for study. This limitation in an unselected group of cases caused this feature to be of diminished value in this study. The examination of the gross specimen removed by total or partial cystectomy would indicate that the application of this feature of invasion is of most value to this group of cases, and is only of limited value in the routine case treated by transurethral resection. The difficulty in exact orientation of these fragments makes this feature of little value unless specimens are carefully taken from various portions of the wall, kept in separate containers and properly labeled for histological study.

For clinically grade 1 tumors, transurethral resection and fulgurization is at present the treatment of choice. No indication was found for more radical therapy. Moderate success with transurethral resection and fulguration, suprapubic cystotomy and electrocoagulation, and partial cystectomy was obtained in the clinically grade 2 tumors. It is thought that total cystectomy would not have improved the results in this group. Only occasional satisfactory responses were obtained in the grade 3 tumors regardless of the method of therapy used. Total cystectomy might be of limited value in the grade 3 tumors. Patients with grade 4 tumor received only palliative treatment with questionable results. Radium and deep x-ray therapy were not utilized in enough cases in this series to be informative.

CONCLUSION

The clinical and pathological features of 96 consecutive cases of malignant neoplasms of the urinary bladder have been reviewed. The histological classification, clinical grading, microscopic grading and invasiveness of the neoplasm have been analyzed. In determining the prognosis of cases of transitional cell carcinoma the most reliable and applicable criteria are a combination of the clinical grade of the neoplasm and its histological features. This fact is supported by the follow-up studies of 92 of these patients.

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POTENTIAL ERRORS IN TOTAL CYSTECTOMY—A PLEA FOR CONSERVATISM

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Recent enthusiasm for radical surgery has stimulated the use of cystoprostatectomy for vesical neoplasm.[1, 2, 3, 4] Total extirpation while sound in theory has failed to cure many bladder cancers. Survivors of the disease and treatment, too often have had severe disability incident to cloaca creation. It has been well established that 60 per cent of all vesical lesions are cured or controlled by skillful transurethral resection.[5, 6, 7] The authors desire to present 4 case reports illustrative of the cure of advanced vesical malignancy with the resectoscope After transurethral resection, total cystoprostatectomy was completed in three and advised in the fourth. In most situations, grading of the degree of malignancy is the province of the pathologist. Carcinoma of the bladder is the chief exception.[8] [9] [10] [11] [12] Experience of urologists generally indicates that the practiced cystoscopic eye estimates the degree of invasiveness more accurately than does microscopy. Despite experience of the cystoscopist and his tactile perception combined with the pathologist's evaluation, grave errors can occur. This paper presents four such mistakes in judgment. Radical surgery for incurable lesions is bad enough, but the anatomic and likely physiologic disturbance of an individual, for lesions curable by lesser means, indicates hesitation should be employed in this approach. Review of the literature reveals eleven recent cases wherein thorough transurethral resection proved invasive bladder neoplasm.[13] [14, 15] [16] [17] [18, 19] The clinical and pathological findings in these patients

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met the requirements for ureterosigmoidostomy and cystoprostatectomy. In each radical surgical specimen, the pathologist was unable to find evidence of residual bladder cancer. Comment was focused on the importance of urinary diversion by ureterosigmoidostomy without emphasizing the significance of the previous careful resection of the tumor with fulguration of the base of the tumor and adjacent area. In each of these cases, the patient had been cured of his cancer before his bladder had been sacrificed.

CASE REPORTS

Case 1. B. W. (2717A), a 45-year old white man, was seen on May 21, 1948, for sudden, total, gross hematuria of 1 week's duration. Cystoscopy revealed two areas of flat, apparently infiltrating, tumor on the right lateral bladder wall measuring 1 by 2 cm. each. They were just lateral to the right ureteral orifice and did not interfere with drainage. After deep transurethral resection, the tumor base and adjacent areas were thoroughly fulgurated. Bimanual examination showed no bladder fixation. Histological study showed transitional cell carcinoma of the bladder, grade 2 to 3 (fig. 1, *A*). Experienced urologic opinion indicated an infiltrating lesion. Bilateral ureterosigmoidostomies by the Coffey 2 technique were done on July 7, 1948.[20] Excretory urograms 41 days later showed a normal left kidney and minimal right hydronephrosis and hydro-ureter. Seventy-two days after transurethral resection of the bladder cancer, cystoprostatectomy by the combined abdominoperineal route was performed without incident. Careful histological study of the entire surgical specimen showed no evidence of malignancy. The postoperative course was uncomplicated. Excretory urograms in August 1951, showed normal kidneys and ureters. His electrolyte balance has been normal.

Case 2. A. M. (198746), a 51-year old white man, was first seen in May 1948, for painless, intermittent, gross, total hematuria of 5 months' duration. Cystoscopy revealed multiple flat tumors around the left ureteral orifice and extending along the interureteric ridge. Another tumor, 2 by 3 cm., was located on the bladder neck at 3 o'clock. Transurethral resection of the tumor, prostate, surrounding mucous membrane and underlying tissue was performed. Bimanual examination showed no evidence of extravesical extension. Retrograde pyelograms were normal. Histological study of the biopsies showed transitional cell

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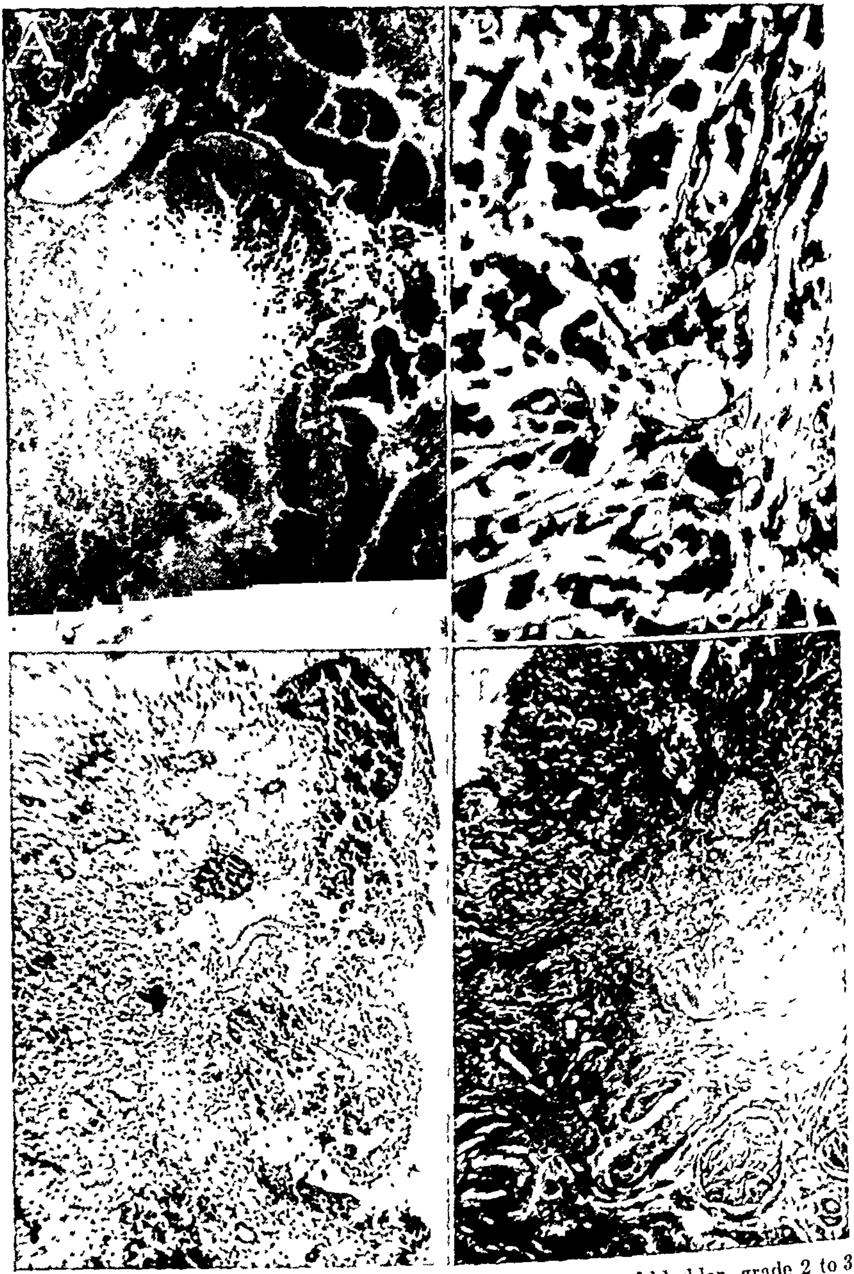

FIG. 1. *A*, B. W. (No. 2717A) transitional cell carcinoma of bladder, grade 2 to 3 *B*, A. M. (198746) transitional cell carcinoma of bladder, grade 1 to 2 *C*, J. A. C (200705) infiltrating transitional cell carcinoma of bladder, *D*, J. J (191519) transitional cell carcinoma of bladder, grade 2.

carcinoma of the bladder grade 1 in malignancy (fig. 1, *B*). Repeated cystoscopic observation suggested that the lesion was infiltrating. Bilateral ureterosigmoidostomies by the Coffey 2 technique were done on June 4, 1948. Total cystoprostatectomy by the combined abdominoperineal route was performed on the twenty-first postoperative day. He was discharged home on his thirty-seventh postoperative day with normal blood chemistry values.

Careful histological study of the entire surgical specimen removed 27 days after transurethral resection of the bladder carcinoma and 21 days after urinary diversion revealed no residual cancer.

Postoperatively, this man has been dependent on society for support. His clinical course has been complicated by recurrent pyelonephritis. In August 1951, excretory urograms showed increased left hydronephrosis. The blood urea nitrogen was elevated to 30 mg. per cent; the carbon dioxide combining power was 20 to 26 volumes per cent. Left neo-ureterosigmoidostomy by the Cordonnier technique gave complete relief from infection and temporary return to normal blood chemistry.[21] Excretory urography in February 1952, showed bilateral hydronephrosis, grade 1 and 2, with two hour retention of dye on the left. Asymptomatic, mild uremia and hyperchloremic acidosis had returned. He expired in the hospital in June 1952, of severe electrolyte imbalance. For the previous 3 months his paranoid behavior had menaced his family and friends. Autopsy showed no cancer.

Case 3. J. A. C. (200705), a 60-year old white man, was first seen on February 8, 1951, for gross, total hematuria and irritative bladder symptoms of 3 months duration. Cystoscopy and resection elsewhere, on February 4, 1951, showed a beefy, red, papillary and edematous trigone, with a highly malignant, infiltrating carcinoma of the bladder. Thorough resection of the trigone, surrounding mucous membrane and underlying tissue on February 12, 1951, showed persistence of infiltrating bladder carcinoma (fig. 1, *C*). Bimanual examination showed no evidence of extravesical fixation. Cystoscopic observation indicated radical treatment.

Bilateral ureterosigmoidostomies by the Coffey 2 technique were done on February 27, 1951. The immediate postoperative course was accompanied by moderate, recurrent bilateral pyelonephritis. Blood biochemical patterns were normal except for elevations of the blood urea nitrogen to 42.0 mg. per cent. Excretory urography 14 days after ureterosigmoidostomy showed delayed function, and bilateral hydronephrosis, grade 2 in degree.

Because of the stormy postoperative course, total cystoprostatectomy by the combined abdominoperineal route was not performed until April 24, 1951. There was no evidence of extravesical extension of the bladder neck neoplasm. Before and after total cystectomy, hyperchloremic acidosis was evident and persisted despite all efforts to restore normal blood chemistry. His carbon dioxide combining power of 17 to 22 volumes per cent aggravated his psychogenic vomiting Even 2 gm. of sodium bicarbonate daily orally, or any intravenous alkaline medication, caused prompt ankle edema and pulmonary congestion. He was discharged on his eighteenth postoperative day after total cystoprostatectomy.

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ABSORPTION OF WATER, UREA, GLUCOSE AND ELECTROLYTES THROUGH THE HUMAN BLADDER

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An elderly patient (P. H. No. 94-28-26) in severe congestive cardiac failure and on a low-NaCl diet was transferred to us from the Medical Service for obstructive hypertrophy of the prostate. He had an indwelling catheter and was accompanied by orders to irrigate the bladder twice daily with distilled water rather than with isotonic NaCl. The nurses called our attention to this order and queried us. After a thorough survey of the literature we still could not answer definitely whether isotonic NaCl is absorbed through the bladder. Thus this investigation was initiated.

MATERIALS AND METHODS

It was not long before a natural opportunity to test the absorptive properties of the normal or near-normal human bladder occurred. A 59-year-old Caucasian male (P. H. No. 01-25-91) underwent a bilateral ureterosigmoidostomy in preparation for a total cystectomy to be done at a later date. The reason for cystectomy was a recurrent, very small papillary tumor of the trigone. This was excised for biopsy and found not to have invaded the submucosa. It was excised by a small biopsy forceps 30 days before the first physiological measurements were made and the small defect in the vesical wall had epithelialized at the time of the measurements. This was confirmed by the pathological report of the entire bladder which was removed ten days after the first measurement and three days after the last. The pathological report, by Drs. M. M. Melicow and J. M. Waldrep, indicated the following abnormalities: "Mucosa of lower left lateral aspect and left portion of trigone shows reddish discoloration; no papillary projections. In a small area the mucosal lining is thin and the arrangement of the cells is not orderly and they vary in size; no submucosal invasion although there are numerous lymphocytes below this area." The diagnosis was "intramucosal epithelioma of bladder" in a small area. There was thus a practically normal bladder from the standpoint of absorption. The above low-grade "reddish discoloration" in a small area was doubtless caused by the daily catheter used in the experiments. Furthermore, a low-grade, non-extensive inflammation was desirable since it would more nearly approach the condition in bladders with residual urine in which absorption of materials from the "dead-space" urine might be significant.

Various solutions of accurately measured volume were introduced into the bladder through an indwelling 24 or 26F (i.e., 24 or 26 mm. in circumference) urethral whistle-tip catheter taped in place and clamped. This method was futile as the bladder underwent spontaneous contractions, especially when the patient had a bowel movement, and usually expelled urine around the clamped catheter. These contractions, which were found to produce intravesical pressures

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of 180 mm. Hg. (243 cm. of water), caused severe discomfort referred to the shaft of the penis. This was true even when the catheter was properly placed, i e., with its orifices close to the vesical neck. Owing to the ureterosigmoidostomy the patient had bowel movements about every 3 hours and we wished the solutions to remain in the bladder for about 4 hours. "Paregoric," "kalpec," and banthine had no striking assuaging effect.

The catheter (fig. 1, *C*) was thus not clamped but connected with a mercurial manometer, *M*, by means of narrow polyethylene tubing (*P*) from an Abbott intravenous set. The solution was slowly introduced into the bladder through a small Y-tube (*T*) after clamping off *P* by *Y*. The solution introduced was accurately measured in the 50 cc syringe, *S*. After the desired amount of solution was introduced (usually 50 cc but sometimes 90 cc), clamp *Z* was shut, clamp *Y* opened, and the syringe removed. Owing to the density of mercury, vesical contractions could move the solution only a small distance into *P*; during vesical relaxation the solution was drawn back into the bladder. This permitted a mobile system without physiological objections. Under such circumstances, the patient experienced no discomfort during the occasional vesical contractions. In most instances only 50 cc of solution were used because they caused less vesical contractions than 90 cc. The patient's bladder capacity was about 200 cc.

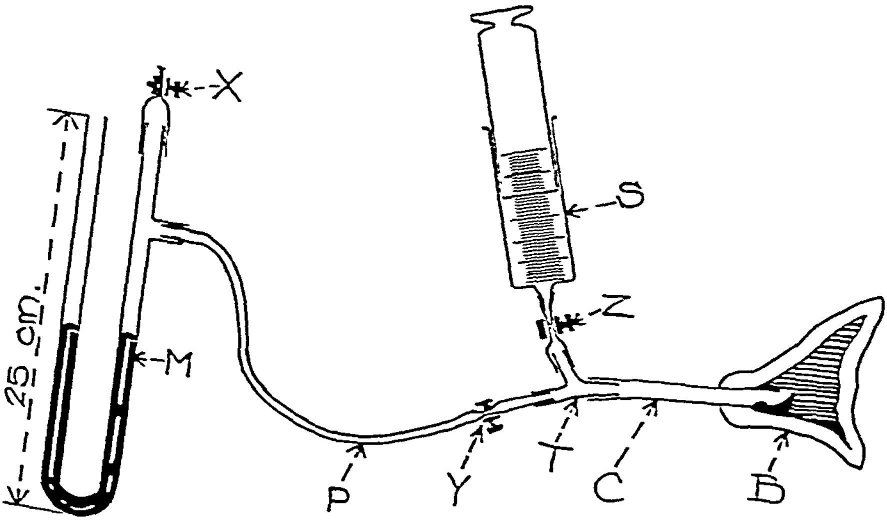

FIG. 1. Apparatus for measurement of absorption through human bladder. *B*, bladder partially filled with liquid; *C*, 26F whistle-tip urethral catheter; *M*, mercurial manometer 25 cm. long; *P*, polyethylene tubing from Abbot intravenous sets; *S*, 50 cc syringe with plain nozzle; *T*, narrow T-tube or Y-tube; *X*, clamp; *Y*, clamp; *Z*, clamp.

Before attaching the manometer to the urethral catheter (26F whistle-tip) the bladder was irrigated a few times with the solution to be used that day. All of the irrigating solution was then withdrawn from the bladder by injecting some air and sucking back. With the whistle-tip catheter taped to the penis so that the orifices were close to the vesical neck it was repeatedly shown that the amount of liquid introduced into the bladder could be recovered within 0.5 cc (1 per cent error). A trace of methylene-blue in the solution showed that no losses occurred by expulsion around the catheter. The bladder formed no exudate as shown by complete lack of any fluid upon introducing the catheter on the day of experiment and sucking back after introducing air by syringe. The solutions were at room temperature (about 20°C) and their volumes measured after they had returned to room temperature upon recovery from the bladder. Since distilled water may be nocuous to the vesical mucosa it was used last. The solutions were kept in the bladder approximately 4 hours and the catheter was removed at the end of that time. The patient was in good general health and co-operative.

The analyses of the initial and final concentrations were always run simultaneously to circumvent slight errors which may result from technique. The sodium and potassium values were established by flame-photometry. The total amount of any substance contained in the bladder at any time was, of course, equal to the concentration times the volume. This product was always used when determining the amount of substance absorbed.

RESULTS

1. Diffusion of sodium, chloride, and water. Ninety cubic centimeters of somewhat hypertonic (about 2 per cent) NaCl were introduced into the bladder (0.94 per cent NaCl is isotonic with the plasma). At the end of 4 hours 98 cc were recovered.

The results were as follows:

Total mEq. in bladder

	INITIAL	FINAL	AMOUNT ABSORBED
Na^+	33.4	31.2	2.2
Cl^-	30.8	28.6	2.2

A repeat performance the next day was done. Fifty cubic centimeters of 2 per cent NaCl were introduced. At the end of 4 hours 54 cc were recovered.

Total mEq. in bladder

	INITIAL	FINAL	AMOUNT ABSORBED
Na^+	17.6	16.9	0.7
Cl^-	17.4	16.7	0.7

Another repeat experiment was done on another day, in which 50 cc of ca. 2 per cent NaCl were introduced into the bladder. At the end of 4 hours 52 cc were recovered. This time the concentration of K^+ in the final fluid was measured to note if K^+ diffuses into the bladder fluid.

Total mEq in Bladder

	INITIAL	FINAL	AMOUNT ABSORBED
Na^+	18.9	16.4	2.5
K^+	0 00	0.050	-0.050
Cl^-	17.2	14.5	2.7

Again small amounts of Na^+ and Cl^- were absorbed and water diffused into the bladder. A trace of K^+ appeared in the vesical fluid; the actual *concentration* of this was only 1.0 mEq/l, i.e., ⅕ of that in the plasma.

Thus a slight amount of Na^+ and Cl^- can diffuse into the blood from a hypertonic solution. Simultaneously water diffuses into the bladder tending to make the intravesical fluid isotonic with plasma. It was not thought worthwhile to emphasize what percentage of the total was absorbed in 4 hours as this would probably depend upon several variables: volume of fluid in bladder, extent of stretch of the vesical wall, initial concentration of the substance, and so on.

2. Diffusion of potassium. Ninety cubic centimeters of somewhat hypertonic (ca. 2 per cent) KCl were introduced into the bladder (1.21 per cent is isotonic with the plasma). At the end of 4 hours 98 cc were recovered.

The results were as follows:

Total mEq. in bladder

	INITIAL	FINAL	AMOUNT ABSORBED
K^+	24.9	24.7	0.2
Cl^-	23.3	24.3	−1.0

Thus, only a trace of the K^+ was absorbed and this may be within the limits of of error as no Cl^- absorption occured. On the other hand, the speed of water diffusion into the bladder is quite as high as with hypertonic NaCl.

3. Diffusion of sodium and chloride from isotonic solutions. Fifty cubic centimeters of "isotonic" NaCl (Abbott) were introduced into the bladder. Fifty-one cubic centimeters were recovered at the end of 4½ hours.

The results were as follows:

Total mEq. in bladder

	INITIAL	FINAL	AMOUNT ABSORBED
Na^+	8.45	8.50	−0.05
K^+	0.00	0.060	−0.060
Cl^-	7.51	7.40	0.11

It is apparent that practically no Na^+ or Cl^- is absorbed from an isotonic solution. Incidentally, a trace of K^+ diffused into the intravesical fluid. The use of isotonic NaCl to irrigate the bladders of patients on the strictly low-NaCl diet is thus not contra-indicated. In the experiment on the diffusion of dextrose (below) it will be noted that practically no Na^+ or Cl^- was absorbed from the glucose in "isotonic" NaCl.

4. Diffusion of urea. Fifty cubic centimeters of a somewhat hypertonic urea (ca. 2 per cent) were introduced into the bladder (1.8 per cent is isotonic with the plasma). At the end of 4 hours 50 cc were recovered. The initial concentration of urea as measured by analysis was 1.95 per cent and the final concentration 1.19 per cent. The volume of water in the bladder remained constant.

The amount of urea absorbed from this hypertonic solution was 56 mg. per hour. Traces of Na^+, K^+, and Cl^- were lost into the intravesical fluid.

Total amounts in bladder

	INITIAL	FINAL	AMOUNT ABSORBED
Urea	975 mg.	750 mg.	225 mg.
Na^+	0.00	1.0 mEq.	−1.0 mEq.
K^+	0.00	0.055 mEq.	−0.055 mEq.
Cl^-	0.00	0.83 mEq.	−0.83 mEq.

The experiment was repeated with similar results. Again 50 cc of 2 per cent urea were introduced and 50 cc recovered after 4 hours.

5. *Diffusion of dextrose.* Fifty cubic centimeters of ca. 5 per cent dextrose in "isotonic" NaCl (Abbott) were introduced into the bladder. After 4 hours 58 cc were recovered.

The results were as follows:

Total amounts in bladder

	INITIAL	FINAL	AMOUNT ABSORBED
Dextrose	2.20 gm.	2.20 gm.	0.0 gm.
Na^+	9.1 mEq.	8.7 mEq.	0.4 mEq.
K^+	0.00 mEq.	0.064 mEq.	−0.064 mEq.
Cl^-	7.40 mEq.	7.45 mEq.	−0.05 mEq.

No dextrose or Cl^- was absorbed. The amount of Na^+ absorbed may have been within the limits of error as indicated by lack of corresponding absorption of Cl^-. A trace of K^+ was lost into the intravesical fluid.

The next experiment (No. 6, on the absorption of distilled water) will show that dextrose does not diffuse from blood into intravesical fluid even when the concentration in the blood is raised artificially.

6. *Absorption of distilled water.* Fifty cubic centimeters of distilled water were introduced into the bladder at 1845 o'clock. At 2100 o'clock intravenous drip of 1000 cc of 10 per cent dextrose was begun. At 2300 o'clock all the 1000 cc had just run in and at that time the venous blood-sugar, drawn from the opposite arm, was 360 mg. per cent, at which time also 40 cc of liquid could be recovered from the bladder; none was lost in the interim. By Benedict's qualitative test there was not a trace of reducing substances in the bladder-fluid.

The results were as follows:

To'al in bladder

	INITIAL	FINAL	AMOUNT ABSORBED
Glucose	0.00 gm.	Less than trace (0.020 gm.)	0.00
Na^+	0.00	0.32 mEq.	−0.32 mEq.
K^+	0.00	0.048 mEq.	−0.048 mEq.

Thus, plain water diffuses rather freely through the vesical wall when it has no osmotically active substance. Dextrose does not diffuse from blood into the intravesical fluid even when its concentration is markedly raised in the blood by intravenous administration. Traces of Na^+ and K^+ are again found to escape into the intravesical fluid when the latter is lacking these initially.

LITERATURE AND DISCUSSION

Probably the first experimental study on the absorption of material from the bladder was that by d'Etchepare (1824) who instilled a dilute alcoholic extract of the strychnine plant into the bladder of a dog. After 20 minutes the dog was in convulsions and death followed. While a medical student in Tübingen, Kaupp (1856) kept himself on a constant diet and noted the concentration of urea and salts in his bladder after refraining from micturition for 1 hour and 12 hours. After doing this for several months he concluded that both urea and salts are reabsorbed from the bladder.

The old works are difficult to appraise because of the relatively crude methods of quantitative analysis and the high concentrations of substances used in the bladder. Gerota (1897) reviewed the preceding literature in detail and used anesthetized female cats and dogs since it was easy to ligate the urethra at the vesical neck in these animals. The ureters were ligated close to the bladder carefully avoiding damage to arteries which enter the bladder. Solutions were introduced into the bladder by urethral catheter, through a ureteral stump, or directly by needle-puncture. He used relatively high concentrations such as 10–16 per cent glucose or urea and noted evidence of slow absorption of both substances but failed to obtain evidence of absorption of strychnine sulfate or nitrate or of cocaine hydrochloride or atropine sulfate even when these were introduced in toxic amounts into the bladder.

Macht (1918a and b) used unanesthetized male dogs and introduced a catheter into the bladder or only up to the external sphincter. He noted that the absorptive power of the bladder to various alkaloids (apomorphine, morphine, atropine, cocaine, epinephrine, and so on) is very slow while absorption from the prostatic urethra occurs rapidly. The objection to this method is that the urethra, being narrow, would not accommodate to the entrance of a given quantity of fluid and extravasation into urethral venous and lymphatic channels would be likely.

The second extensive review of the literature on the subject appeared by Mann and Magoun (1923) who presented 70 references. They remarked that some of the negative results may have been due to: 1) injury to the blood-supply of the bladder, 2) employment of test-substances which could be detected only with difficulty, and 3) selective absorption through the vesical mucosa. They performed experiments on female dogs under ether using a technique similar to that of Gerota (above). The volume they introduced into the bladder was about $\frac{1}{5}$ of the vesical capacity. They noted that traces of phenolsulfonphthalein (P.S.P.), methylene blue, and indigo carmine are absorbed from the bladder as indicated by their appearance in the ureteral urine. Vickers and Marshall (1924) presented evidence that urea and NaCl are absorbed from the bladder of rabbits under urethane and ether anesthesia. So (1927) introduced 1 gm. urea per kg. into the bladder of rabbits which had had both ureters ligated close to the bladder. The blood-urea concentration rose. Similar results were obtained with glucose, 2 gm./kg. On the other hand, proteins such as agglutinins, precipitins, and he-molysins apparently were not absorbed as antibodies were not produced in the plasma except for sheep-hemolysin. Bacteria, such as Esch. coli and Proteus vulgaris, were not absorbed. Cystitis produced by introducing a sublethal dose of cantharidin into the bladder allowed a generalized blood-invasion with Proteus but not with E. coli. Frogs are capable of forming only a hypotonic urine; when their cloacal aperture is tied while they are immersed in water their increase in weight is mainly due to accumulation of urine in the bladder. Steen (1929) found that when frogs are transferred to a dry chamber or to slightly hypertonic NaCl the contents of their bladder are almost completely reabsorbed. Hudiwara (1931) studied factors in the permeability of the bladder of the toad isolated from the body. Giacobbe and Vitale (1930), using dogs in which the ureters had been divided close to the bladder, noted the absorption of traces of indigo carmine from the bladder as indicated by appearance in the ureteral urine. Bacillus prodigiosus was absorbed into the blood-stream in 3 dogs out of 10. In a paper illustrated by handsome radiographs, Frey (1932) demonstrated the absorption of organic iodides (uroselectan and abrodil) and of NaBr from the bladder of rabbits. Within 1 hour there was appreciable absorption of uroselectan (5–40 per cent used) and abrodil (10–20 per cent used) and NaBr (5–25 per cent used) and the bladder was practically radiolucent in 16 hours. At 1 hour absorption from the bladder was sufficient to produce a pyelogram. When intravesical tension was greater, as when 8–10 cc were used instead of 4–5 cc, absorption of the aforementioned contrast media was faster. Cocaine, pantocain, and alypin were rapidly absorbed when the bladder was filled. Fender (1934) reviewed the literature and experimented with cats under amytal. He noted an absorption of urea through the bladder but his concentrations were too high (10–50 per cent) and his volumes relatively large (25 cc), which renders his results open to the objection of possible vesical changes by hypertonicity. Hishikawa (1936), using the classical technique, introduced 30 cc of 2 per cent solutions of various dyes into the bladder of rabbits. Urine was collected from the ureters. Phenolsulfonphthalein, eosin, indigo carmine, neutral red, methylene blue were absorbed; the diazo-dyes were not absorbed. Inflammation of the bladder caused by HCl caused permeability to practically all 14 dyes used. Galm and Kraft (1938) noted slow absorption of methylene blue, carmine red, and trypan blue; also of creatinine and uric acid from the bladders of rabbits and dogs. They considered that absorption from the bladder was probably by way of the lymphatics.

The most comprehensive recent work is that of Schär (1938) on dogs and rabbits. Sodium iodide, glucose, urea, and methylene blue were absorbed. He introduced 30 cc of urine into an emptied bladder and after 24 hours noted a marked fall in the urea, NaCl, calcium, and total volume. The strongly carcinogenic naphthylamines were absorbed. Travell (1940) found that nicotine in the bladder was much more toxic at the higher pH's, at which the concentration of the undissociated base is markedly increased. Burgess et al. (1950, 1951) noted absorption of radioactive phosphate, sulfate, calcium, ionic mercury, and colloidal gold through the canine bladder. Conradt (1937) stands alone among recent workers in denying absorption of water (as distilled water) through the bladder although he notes a slight but definite absorption of urea. He found no appreciable change in the volume or concentration of 0.2 per cent to 0.85 per cent NaCl (all hypotonic) introduced into the canine bladder.

There are a number of reports concerning absorption of substances through the human bladder. Schär (1938) introduced 50 cc of 1–2 per cent NaI into the bladder by catheter. After 60 minutes the total amount of NaI in the bladder was measured. Indigo carmine 4 per cent and 0.1 per cent nupercaine were similarly studied. In all cases absorption was appreciable. More was absorbed from inflamed than from normal bladders. Isotonic NaCl was introduced into the bladder of a patient completely anuric from $HgCl_2$ poisoning, whose blood (urea) was 250 mg. per cent. After 30 minutes the solution in the bladder contained 30 mg. per cent urea. Similar results were obtained in a patient anuric from shock. De la Peña (1928) and Baretz, Harten, and Walzer (1943) reported absorption of allergins (protein) from the normal human bladder. Lundberg (1929) introduced 10 per cent LiI into the bladder with both ureters catheterized. Within 15 minutes both the ureteral urine and the saliva simultaneously contained iodine. Harild (1935) noted slight but significant absorption of nupercaine through the human bladder and urethra: 0–4 per cent in 15 minutes. Tumor or cystitis augmented the absorption. Rupel and Harger (1937) quantitated the amount of cocaine absorbed through the human urethra and bladder. Steller and Vondra (1941) introduced 100 cc of 2–20 per cent urea into the human bladder with ureteral catheters in situ. Blood samples were drawn before and during the experiment (1 to 3 hours). Only 10 per cent of the 25 patients showed elevations in blood (urea). This method does not take into consideration the fact that the kidneys can excrete urea rapidly and would thus prevent a rise in blood (urea) provided the rate of absorption did not exceed a certain unknown value. Moritz and Jetter (1942) noted that ethyl alcohol can diffuse through the human bladder in either direction in life or death.

So far as is known, nobody has found how rapidly urea can be run into the bloodstream without raising the blood-[urea] in a person with normal kidneys. This may be due to the toxic impurities in preparations of urea preventing its intravenous use. It is probable that a person with normal kidneys can receive considerably over 56 mg. of urea into his bloodstream per hour (the rate we found here) without appreciable rise in his blood-[urea]. This would explain how a patient who carries a large urinary residual in his bladder often has a normal blood-[urea] even though, as we believe, he reabsorbs an appreciable amount of urea through his bladder. If his kidneys function subnormally and if he has cystitis, the reabsorption of urea through his bladder may be responsible for a rise in blood-[urea], i.e., for the *empoisonnement urineux* of Fey (1936). The data here indicate that one need not worry about K^+-reabsorption through the bladder and that the bladder of a patient in severe congestive cardiac failure can be irrigated with isotonic NaCl without fear of Na^+ or Cl^+ absorption.

SUMMARY

An approximately ideal occurrence permitted this study. A patient from whose bladder a small recurrent papilloma had been fulgurated a few weeks previously had undergone a bilateral ureterosigmoidostomy in preparation for cystectomy

molysins apparently were not absorbed as antibodies were not produced in the plasma except for sheep-hemolysin. Bacteria, such as Esch. coli and Proteus vulgaris, were not absorbed. Cystitis produced by introducing a sublethal dose of cantharidin into the bladder allowed a generalized blood-invasion with Proteus but not with E. coli. Frogs are capable of forming only a hypotonic urine; when their cloacal aperture is tied while they are immersed in water their increase in weight is mainly due to accumulation of urine in the bladder. Steen (1929) found that when frogs are transferred to a dry chamber or to slightly hypertonic NaCl the contents of their bladder are almost completely reabsorbed. Hudiwara (1931) studied factors in the permeability of the bladder of the toad isolated from the body. Giacobbe and Vitale (1930), using dogs in which the ureters had been divided close to the bladder, noted the absorption of traces of indigo carmine from the bladder as indicated by appearance in the ureteral urine. Bacillus prodigiosus was absorbed into the blood-stream in 3 dogs out of 10. In a paper illustrated by handsome radiographs, Frey (1932) demonstrated the absorption of organic iodides (uroselectan and abrodil) and of NaBr from the bladder of rabbits. Within 1 hour there was appreciable absorption of uroselectan (5–40 per cent used) and abrodil (10–20 per cent used) and NaBr (5–25 per cent used) and the bladder was practically radiolucent in 16 hours. At 1 hour absorption from the bladder was sufficient to produce a pyelogram. When intravesical tension was greater, as when 8–10 cc were used instead of 4–5 cc, absorption of the aforementioned contrast media was faster. Cocaine, pantocain, and alypin were rapidly absorbed when the bladder was filled. Fender (1934) reviewed the literature and experimented with cats under amytal. He noted an absorption of urea through the bladder but his concentrations were too high (10–50 per cent) and his volumes relatively large (25 cc), which renders his results open to the objection of possible vesical changes by hypertonicity. Hishikawa (1936), using the classical technique, introduced 30 cc of 2 per cent solutions of various dyes into the bladder of rabbits. Urine was collected from the ureters. Phenolsulfonphthalein, eosin, indigo carmine, neutral red, methylene blue were absorbed; the diazo-dyes were not absorbed. Inflammation of the bladder caused by HCl caused permeability to practically all 14 dyes used. Galm and Kraft (1938) noted slow absorption of methylene blue, carmine red, and trypan blue; also of creatinine and uric acid from the bladders of rabbits and dogs. They considered that absorption from the bladder was probably by way of the lymphatics.

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UNSUCCESSFUL ATTEMPTS TO PRODUCE OSTEITIS PUBIS IN DOGS

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A review of the literature suggests simple electrocoagulation or else injury to the obturator nerve might play a part in the etiology of osteitis pubis.

The first case of osteitis pubis following the use of electrofulguration was reported by Bucalossi in 1935. The operation in this instance was a suprapubic removal and fulguration of a bladder neoplasm on which two previous transurethral electrofulgurations had been done. Wheeler then reported the occurrence of osteitis pubis following transurethral electroresection of the prostate in a patient who also had required a suprapubic cystotomy for the control of bleeding induced during the first procedure. In the case reported by Bruskewitz and Ewell, considerable difficulty was encountered in controlling bleeding from the anterior lobe during a transurethral resection of the prostate, necessitating extensive electrofulguration of the roof of the prostate. No open operation had been performed on this patient. Moore reported a 17 per cent incidence of osteitis pubis in his first series of 46 retropubic prostatectomies, and none in his next 70 cases. The difference in technique was that the hemostasis of the prostatic veins in the latter series was accomplished by ligature instead of electrocoagulation.

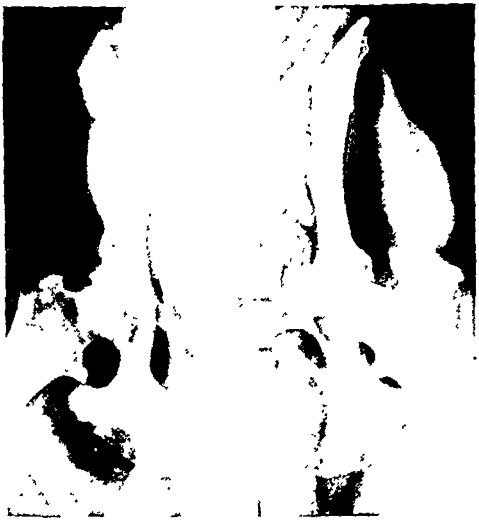

FIG. 1. X-ray of pelvic bones and pubis of a dog taken 10 weeks after deep electrofulguration of periosteum of pubic bone and fibrocartilaginous symphysis. No evidence of osteitis pubis or any type of bone disease. Similar negative x-rays were obtained in other 2 dogs.

The production of osteitis pubis as a result of obturator trauma is theoretically

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His bladder was essentially normal except for a small area of incipient intraepithelial carcinoma which did not extend into submucosa.

There was no appreciable net diffusion of Na^+, Cl^-, and water through the bladder from an isotonic solution of NaCl.

Na^+ and Cl^- diffused appreciably through the bladder from moderately hypertonic, 2 per cent NaCl. Water, simultaneously, diffused into the bladder.

There was no significant net diffusion of K^+ or Cl^- through the bladder from moderately hypertonic, 2 per cent, KCl.

Urea diffused appreciably through the bladder. From 50 cc of 2 per cent urea in a bladder with a capacity of 200 cc the rate of diffusion was 56 mg. per hour.

Glucose did not diffuse appreciably through the bladder in either direction. To test diffusion of glucose into the bladder, the patient's plasma glucose was raised to 360 mg. per cent by intravenous drip of glucose, and isotonic NaCl was introduced into the bladder.

Traces of Na^+, K^+, and Cl^- diffused into the bladder when the intravesical fluid was totally lacking in these.

Distilled water introduced into the bladder diffused through the same.

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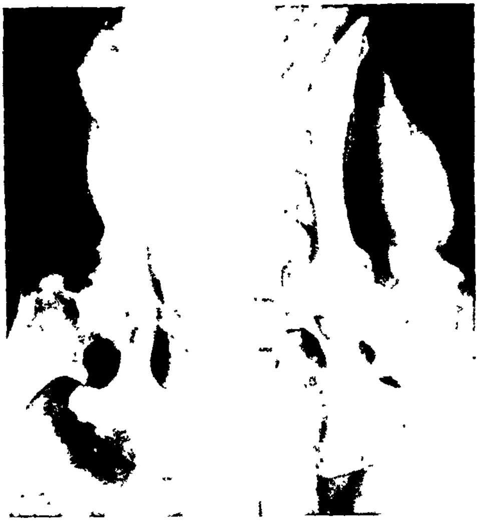

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vague. The term "obturator neuritis," however, has been used to explain many unaccountable pelvic girdle complications following prostatectomy especially when x-ray findings were negative.

MATERIALS AND METHODS

Three dogs were used. In each instance the bladder was opened at the time of surgery to permit free seepage of urine around the bladder. The wounds were closed without drainage.

In the first animal the right obturator nerve, just before it entered the obturator foramen, was irritated by rubbing it with a dry gauze for one minute. A loose strand of 00 chromic catgut was then tied around it and left in place to produce further irritation of the nerve.

In the second dog, the periosteum of the posterior aspect of the pubic bones was soundly fulgurated. Bladder urine was then permitted to bathe this thoroughly burned area.

In the third dog a large wedge of fibrocartilage was excised from the symphysis pubis and urine was again poured over the area.

X-rays of the pelvis were taken at 3 week intervals for a period of 4 to 5 months. No evidence of osteitis pubis was apparent.

DISCUSSION

The only work dealing with experimental animals in attempting to produce osteitis pubis was that of Wheeler in 1941. Trauma, urine and infection were employed to incite bone rarifaction in rabbits.

This is a report dealing with dogs in which electrocoagulation of the pubic periosteum, excision of part of the symphyseal fibrocartilage and irritation of the obturator nerve was used as inciting causes in an unsuccessful attempt to produce osteitis pubis.

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TRANSURETHRAL RESECTION OF THE PROSTATE

EDWARD H. RAY

This discussion is based on personal experiences with 1145 transurethral resections of the prostate in the 5-year period 1946 to 1950 inclusive. These were consecutive cases on patients whose ages varied from 48 years to 91 years, many representing the worst possible risks because of renal damage, urinary sepsis and serious degenerative diseases. A good many were operated upon between coronary attacks and after cerebral vascular accidents associated with severe hypertension. All deaths occurring in the hospital after surgery for whatever reason were accepted as operative deaths and of these there were twelve, an operative mortality of 1.04 per cent.

The purpose of this paper is to remind that transurethral resection of the prostate is a good and relatively safe operation and well worth learning to do well. It seems that there is some danger that the younger urologists and those now in training may neglect to perfect themselves in the technique of the transurethral procedure because the open operations are easier to do and are much more satisfactory now than formerly, due as much to the development of the antibiotics as to any improvement in technique.

Retropubic prostatectomy and suprapubic prostatectomy, as a result of better control of infection and a better understanding of physiology, have become satisfactory procedures, but with an operative mortality in large series of approximately 4 per cent. Twenty years ago the high mortality and high morbidity attendant upon the open enucleation of the prostate placed the urologist under great compulsion to seek a safer method and as a result the transurethral operation was developed. The greatly improved results now obtained by the retropubic and the suprapubic methods have in considerable degree reduced that compulsion and it is for this reason that I fear that many urologists now in training will not have the patience to develop themselves in the technique of the transurethral operation.

Millin at one time said: "Do not think that we have abandoned the transurethral route. We use it in the nonagenarians and some others," and when it is realized that the transurethral operation usually carries the added burden of extraordinary risk from extreme old age, debility and serious cardiovascular disease the lower mortality would seem to be all the more remarkable.

The greatest criticism of the transurethral method has been that there is a greater incidence of recurrence of obstruction after it than after the enucleation methods and this is true, yet it has been my experience that those patients who have such recurrences usually return promptly, submit readily to further resection and usually get along as well as if not better than they did the first time.

Recurrence of obstruction also occurs following the various other methods of removal and this is due to the growth potential that exists in the capsule. Har-

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Read at annual meeting, Southeastern Section, American Urological Association, Memphis, Tenn., March 8, 1951.

vague. The term "obturator neuritis," however, has been used to explain many unaccountable pelvic girdle complications following prostatectomy especially when x-ray findings were negative.

MATERIALS AND METHODS

Three dogs were used. In each instance the bladder was opened at the time of surgery to permit free seepage of urine around the bladder. The wounds were closed without drainage.

In the first animal the right obturator nerve, just before it entered the obturator foramen, was irritated by rubbing it with a dry gauze for one minute. A loose strand of 00 chromic catgut was then tied around it and left in place to produce further irritation of the nerve.

In the second dog, the periosteum of the posterior aspect of the pubic bones was soundly fulgurated. Bladder urine was then permitted to bathe this thoroughly burned area.

In the third dog a large wedge of fibrocartilage was excised from the symphysis pubis and urine was again poured over the area.

X-rays of the pelvis were taken at 3 week intervals for a period of 4 to 5 months. No evidence of osteitis pubis was apparent.

DISCUSSION

The only work dealing with experimental animals in attempting to produce osteitis pubis was that of Wheeler in 1941. Trauma, urine and infection were employed to incite bone rarifaction in rabbits.

This is a report dealing with dogs in which electrocoagulation of the pubic periosteum, excision of part of the symphyseal fibrocartilage and irritation of the obturator nerve was used as inciting causes in an unsuccessful attempt to produce osteitis pubis.

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TRANSURETHRAL RESECTION OF THE PROSTATE

EDWARD H. RAY

This discussion is based on personal experiences with 1145 transurethral resections of the prostate in the 5-year period 1946 to 1950 inclusive. These were consecutive cases on patients whose ages varied from 48 years to 91 years, many representing the worst possible risks because of renal damage, urinary sepsis and serious degenerative diseases. A good many were operated upon between coronary attacks and after cerebral vascular accidents associated with severe hypertension. All deaths occurring in the hospital after surgery for whatever reason were accepted as operative deaths and of these there were twelve, an operative mortality of 1.04 per cent.

The purpose of this paper is to remind that transurethral resection of the prostate is a good and relatively safe operation and well worth learning to do well. It seems that there is some danger that the younger urologists and those now in training may neglect to perfect themselves in the technique of the transurethral procedure because the open operations are easier to do and are much more satisfactory now than formerly, due as much to the development of the antibiotics as to any improvement in technique.

Retropubic prostatectomy and suprapubic prostatectomy, as a result of better control of infection and a better understanding of physiology, have become satisfactory procedures, but with an operative mortality in large series of approximately 4 per cent. Twenty years ago the high mortality and high morbidity attendant upon the open enucleation of the prostate placed the urologist under great compulsion to seek a safer method and as a result the transurethral operation was developed. The greatly improved results now obtained by the retropubic and the suprapubic methods have in considerable degree reduced that compulsion and it is for this reason that I fear that many urologists now in training will not have the patience to develop themselves in the technique of the transurethral operation.

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rison and Poutasse from the Harvard Medical School and Peter Bent Brigham Hospital in a report on 21 recurrences of bladder neck obstruction found that six had had suprapubic prostatectomy, five had had perineal prostatectomy and ten had had transurethral resection. Three of the 6 recurrences after suprapubic prostatectomy proved to be carcinomatous although none had shown any evidence of carcinoma at the time of the original operation. Two of the five recurrences following perineal prostatectomy for benign hyperplasia proved to be carcinoma. This, of course, proves nothing except that prostatic growth and development may continue after any method of removal and that the enucleation operations do not insure against the subsequent development of carcinoma.

It seems to me that the lower operative mortality of transurethral resection more than compensates for the greater incidence of recurrence of obstruction.

As to the technique of the transurethral operation, the importance of thoroughness should be emphasized for complete removal of all prostatic tissue down to the capsule should be the goal at each operation. This is not difficult to accomplish in the smaller and medium sized prostates but may be impossible in the very large ones with the lateral lobes projecting rectalward. Nevertheless, a finger in the rectum to elevate these lateral lobes before the resectoscope will enable the operator to so excavate them that the patient will be thoroughly relieved of his obstruction. Even in the smaller prostates before considering the resection complete a finger should be introduced into the rectum to discover and to elevate any remaining resectable masses of tissue which will usually be found at or near the apex. If this is done and if in appropriate cases the resection is carried all the way through the hypertrophied and sometimes bar shaped trigone of the bladder the postoperative morbidity from continuing slowness of the stream, retention of small amounts of urine and infection will be greatly reduced.

As one increases the thoroughness with which one does a transurethral resection the danger of perforation and extravasation increases. In my experience, this has always occurred posteriorly beneath the urethral edge of the trigone and has been easily recognized by the characteristic cob-web appearance of the tissue. The patient although under spinal anesthesia will usually complain of a deep aching pain in the lower abdomen and will have rigidity of the abdominal wall. This complication occurred twice in my series but failed to result in serious trouble because of immediate recognition and paravesical drainage by the suprapubic route.

Anything more than a transitory incontinence of only a few days' duration has not been encountered more than twice in this series. Thoroughness, especially in the important apical region where it is so easy to leave tissue, may lead to greater risk of damage to the external sphincter; yet I believe this danger has been considerably over-rated, and that if one uses great care in this region the sphincter is not likely to be damaged. If the landmarks seem vague the rectal finger will enable one to palpate the edge of the scope just distal to the verumontanum and upward pressure on the prostate will disclose to view the apical margins of the lateral lobes.

Urethral stricture is a postoperative complication and occurs not infrequently.

The three sites where strictures develop with greatest frequency are at the external urethral meatus, in the anterior urethra at about the level of the penoscrotal junction and at the margin of the vesical outlet in that order of frequency in my experience.

Strictures at the meatus usually develop early and while a patient is still under observation and therefore available for early correction. Those occurring in other areas may not show up for months and in a case of contracture of the margin of the vesical outlet sometimes not for several years. The incidence of stricture formation at the meatus has been greatly reduced by doing adequate meatotomy where indicated before introducing sounds or resectoscope and by using no catheter larger than 22F.

Serious contracture of the vesical outlet occurs infrequently but may require resection for relief. Sometimes the ureteral orifices may be found to be drawn into the very margin of the vesical outlet and while every effort has been made to avoid injuring the ureters in such cases it has been necessary occasionally to cut across the ureter or ureters a distance of 1 to 1½ cm. above the meatus in order to obtain an adequate vesical outlet. Since this same maneuver may be carried out either intentionally or inadvertently at the time of the primary resection also, it may be of interest to mention one such patient who several years later developed hydronephrosis from atresia of the lower end of the ureter necessitating nephrectomy.

Another complication of transurethral resection about which much has been written is renal failure from lower nephron nephrosis due to intravascular hemolysis or to the introduction into the blood stream of the products of hemolysis occurring in the bladder and posterior urethra. This has led to the substitution for water as the irrigating medium of glucose solution by Creevy and of glycine by Nesbit but Robbins, Olson and Rolnick express agreement with Biorn and Greene of the Mayo Clinic that the role of intravesical and intravascular hemolysis in the production of post-resection oliguria is small and probably of little significance.

There are three things that may be done towards the prevention of this complication when water is used: 1) maintenance of a stable blood pressure in the patient by careful attention from a competent anesthesiologist; 2) avoidance of excessive water pressure within the bladder and posterior urethra; 3) meticulous control of bleeding during the progress of the operation.

Excessive intravesical pressure may be largely avoided by keeping the water level in the irrigator no more than 2 feet above the level of the bladder and by frequent emptying of the bladder. It is a great temptation to keep on resecting long after the intravesical pressure has become equal to or in excess of the intravenous pressure. That this is so is proven by the flood of venous bleeding that sometimes occurs from what had appeared to be a bloodless field a moment before letting the water out. Careful hemostasis during the progress of the operation while time-consuming and not always entirely possible does reduce the avenues by which foreign material may gain access to the stream and has the added advantage of conserving blood.

In this particular series of 1145 resections in which water was used as the irrigating medium, there was no clinical evidence that this complication had occurred in any case, although undoubtedly hemoglobinemia would have been found to be present in some degree in many of them had laboratory estimates been made.

In conclusion it is believed that the transurethral operation does have an added safety factor over other methods. When done with proficiency it can be applied to all but the very largest prostates with good results, although in such cases it becomes a very tedious and tiresome procedure requiring the exercise of great patience. Recognizing that skill in the open operations may be more easily acquired and on that account that they will be more attractive especially to the younger urologists, I should like to urge them not to neglect the transurethral operation but to persist in its use until it has found its proper place in association with the other procedures. That place, of course, will eventually be dictated by the personal experiences of each individual surgeon.

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A MODIFICATION OF TECHNIQUE FOR ANASTOMOSING MEMBRANOUS URETHRA AND BLADDER NECK FOLLOWING TOTAL PROSTATECTOMY

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The usual type of anastomosis between bladder and urethra following radical removal of the prostate and seminal vesicles for carcinoma by either the perineal or retropubic approach is illustrated in figure 1. Essentially the anastomosis is the same for both types of radical prostatectomy. In many cases two difficulties arose; distortion of the trigone, and traction and tension upon the membranous urethra. It is possible that the method of anastomosis advocated by Vest acted as a tension suture upon the anterior wall of the bladder and thus avoided these complications.

One of us (R. H. F.) in 1946, described a method of ureterovesical anastomosis using a flap of the bladder wall to form a tube that could be connected to a short ureter. Favorable results with this technique prompted us to apply the same procedure in anastomosing the urethra and bladder following total prostatectomy by the retropubic approach. The method is equally applicable to the anastomosis when using the perineal approach.

TECHNIQUE OF PROCEDURE

Parallel incisions on the lateral or anterior wall of the bladder are made about 3 to 4 cm. apart, extending from the bladder neck upward over the bladder wall. The length of the rectangular flap thus formed is governed by the length of the defect that exists between the urethra and bladder. After the flap is formed, its lateral edges are sutured together with interrupted 00 chromic catgut to form a tube. The bladder neck is closed in a transverse direction with interrupted 00 chromic catgut. This helps to draw the base of the tube closer to the bladder neck. It is drawn still closer by also closing the area from which the flap was made in a transverse direction. A Foley catheter is then passed through the urethra into the tube flap and on into the bladder. The bag is inflated, but no traction is exerted on the catheter. When feasible the tube flap and urethra are then sutured together by three interrupted 00 chromic atraumatic sutures placed at the apices of an equilateral triangle and tied. Figures 2 and 3 illustrate the technique of this procedure.

The advantages of this procedure are 1) lack of tension at the junction of the urethra and bladder, 2) preservation of the trigone in its normal surroundings, 3) production of a tube that more nearly approaches the original posterior urethra, 4) no displacement of the membranous urethra, and 5) formation of a well-united and approximated intact urinary tract.

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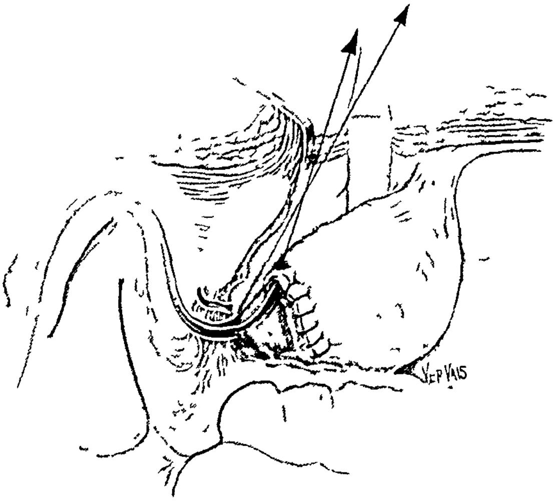

Fig 1 Urethra bladder anastomosis following total retropubic prostatectomy

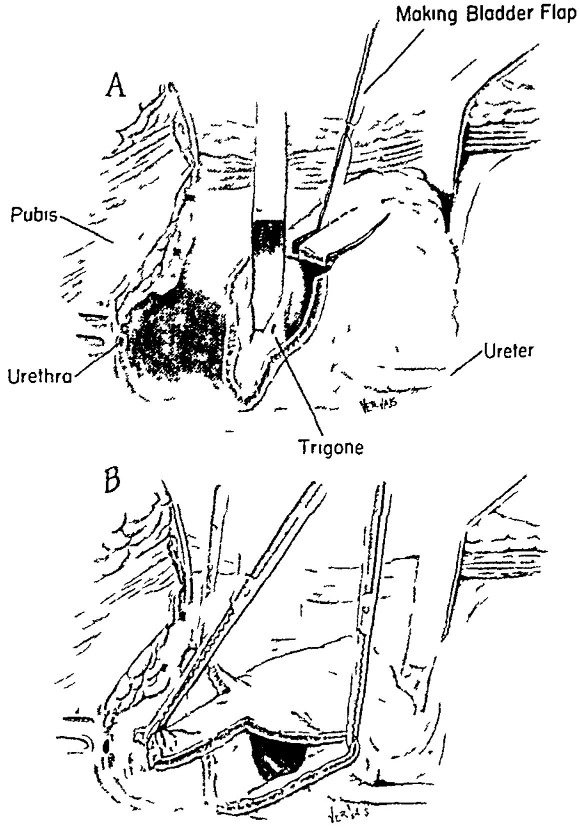

Fig 2 Tube flap urethra bladder anastomosis following total prostatectomy *A*, rectangular flap formed from anterior wall of bladder *B*, flap drawn down to urethra producing lateral recesses at bladder neck

CASE REPORT

The following case illustrates the type of anastomosis which has been described in the foregoing discussion:

P. R., No. 51-9064, was a 73 year old white man who was admitted to the University of Iowa Hospitals with the symptoms of bladder neck obstruction. He had several episodes of complete obstruction and had 250 cc of residual urine on admission. On rectal examination the prostate was found to be one plus enlarged with a hard, fixed nodule on the right lobe. It was about 2 cm. in diameter and seemed to be completely confined within the gland. Biopsies of this area by transurethral and perineal approach were found typical for adenocarcinoma of the prostate. Preoperative cysto-urethrograms revealed a smooth bladder without evidence of reflux or diverticula. The prostatic urethra was straight and narrow (fig. 4, *A* and *B*).

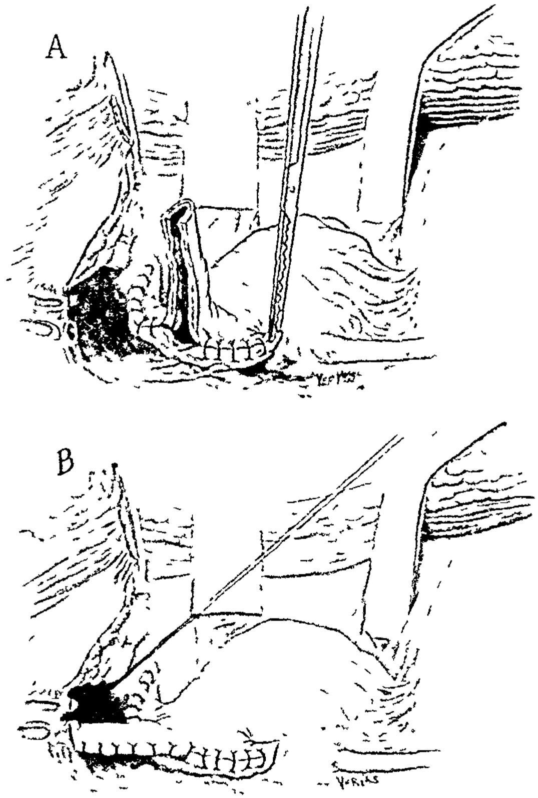

FIG. 3. *A*, bladder neck closes transversely and flap folded upon itself to produce tube. *B*, tube has been formed and sutured to membranous urethra completing anastomosis.

Because the neoplasm seemed to be confined to the prostate gland, a radical retropubic prostatectomy was performed. A block of tissue containing the prostate, seminal vesicles and regional lymphatics was removed. Although this was not a large mass of tissue, a sizable defect was left between the membranous urethra and bladder neck. Attempts to bridge this gap by the previous method of anastomosis would have placed considerable traction on the bladder, tension at the junction of the separated ends of the urethra and bladder, and poor approximation of the components involved in the anastomosis. Therefore, a rectangular tube flap of bladder wall with its base arising on the anterior lateral wall of the bladder was formed, and the anastomosis performed as described

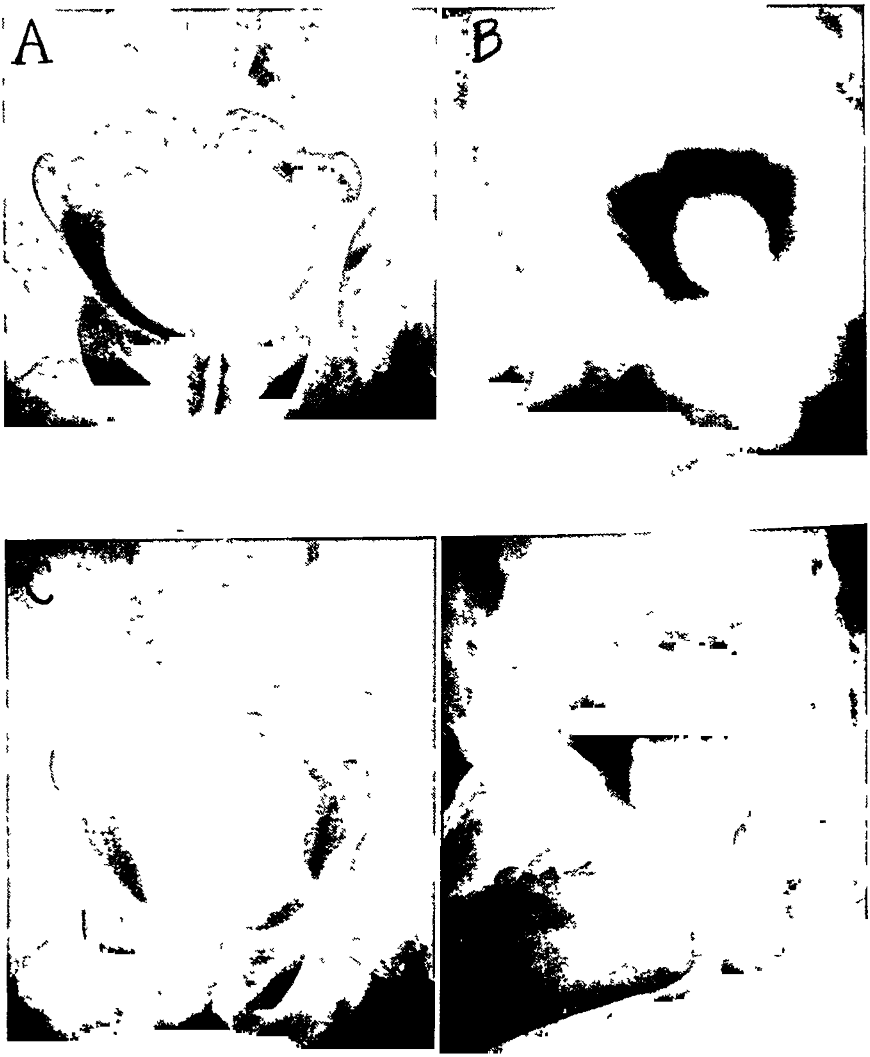

FIG. 4 *A*, preoperative cystogram showing smooth bladder. *B*, preoperative urethrogram showing straight, narrow prostatic urethra. *C*, postoperative cystogram showing pouch on left side of bladder which is produced when bladder is sutured transversely after tube flap is made. *D*, postoperative urethrogram showing normally-appearing posterior urethra

in the preceding paragraphs, without traction at the bladder neck or tension at the site of anastomosis. The urethral catheter was left in place for four weeks. Immediately following the removal of the catheter, the patient had partial stress incontinence, but no dribbling. After three days, he had perfect control of the urinary stream. He carried no residual urine. Postoperative cysto-urethrograms were performed and revealed a smooth adequate bladder neck and urethra (fig. 4, *C* and *D*).

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UNUSUAL CARCINOMAS INVOLVING THE PROSTATE GLAND

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Most general textbooks of pathology do not describe types of prostatic carcinoma other than adenocarcinoma and the somewhat vague scirrhous carcinoma which is probably a variety of adenocarcinoma. Willis,[1] in a treatise on tumors, mentioned the squamous cell type. A rather careful review of the literature revealed only scattered reports, usually of isolated cases, of unusual carcinomas of the prostate. Most of the varieties of carcinoma which we shall consider have been described previously in the literature, but the unusual features in some of the cases we have observed at the Mayo Clinic and the apparent need for emphasis of the fact that not all prostatic carcinomas are adenocarcinomas made this report seem worth while.

SQUAMOUS CELL CARCINOMA APPARENTLY ARISING PRIMARILY IN THE PROSTATE GLAND

In 1926, Spagnol[2] reported a case in which a squamous cell carcinoma apparently arose primarily in the prostate gland. In 1939, Kahler[3] reported 6 cases in which a similar type of tumor was found at necropsy. Since very few cases of this type of tumor have been reported since 1939, the lesion probably is rare. Like similar tumors of the bladder, squamous cell carcinomas of the prostate may show evidence of keratinization, such as the presence of pearly bodies and an abundance of pink-staining cytoplasm (figs. 1 and 2), or there may be little tendency for keratinization to occur (fig. 3).

Seven cases in which a squamous cell carcinoma apparently arose primarily in the prostate gland have been observed at the Mayo Clinic. The clinical and pathologic data in these cases are listed in table 1. Although this series of cases is small, it is significant that the patients lived only a short time after transurethral resection was performed. This type of tumor apparently metastasizes early and grows rapidly. It is interesting to note that in the majority of cases rectal examination revealed an enlarged prostate gland which was soft and presumably not involved by a malignant lesion. The hard consistency of the prostate gland usually noted in cases of carcinoma of this organ was conspicuously absent.

Read at annual meeting, North Central Section, American Urological Association, Toledo, Ohio, October 4 to 6, 1951.

[1] Willis, R. A.: Pathology of Tumours. St. Louis: C. V. Mosby Co., 1948, p. 587.

[2] Spagnol, G.: Epithelioma Pavimentoso Corneificante Primitivo Della Prostata. Pathologica, 18: 590–596, 1926.

[3] Kahler, J. E.: Carcinoma of the prostate gland: a pathologic study. J. Urol., 41: 557–574, 1939.

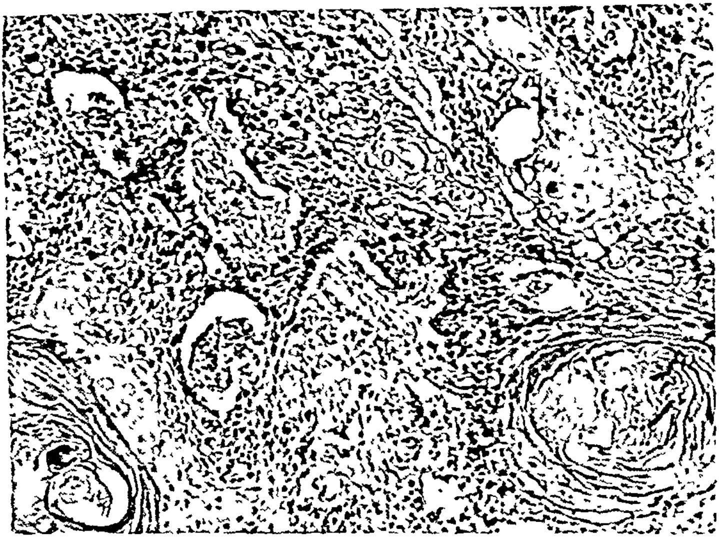

FIG. 1. Squamous cell carcinoma (keratinizing) of the prostate in case 8 (hematoxylin and eosin stain; ×95).

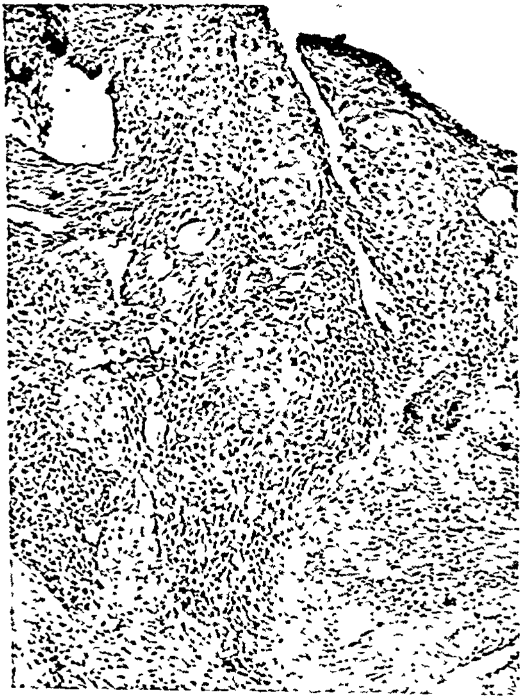

FIG 2 Squamous cell carcinoma (keratinizing) of the prostate in case 15 (hematoxylin and eosin stain; ×80).

Histologically, a squamous cell carcinoma of the prostate is the same as a squamous cell carcinoma of the bladder. Since the latter tumor does not produce acid phosphatase, one would not expect to encounter an increase in the concentration of this enzyme in the serum in a case of squamous cell carcinoma of the prostate. At the time of the initial examination of the patients at the clinic, metastatic involvement (osteolytic) of bone was present in only 1 of the 7 cases, and the concentration of acid phosphatase in the serum was normal in this case. Orchiectomy did not produce any improvement. It seems reasonable to assume that squamous cell carcinomas of the prostate would not be affected by hormonal therapy.[4]

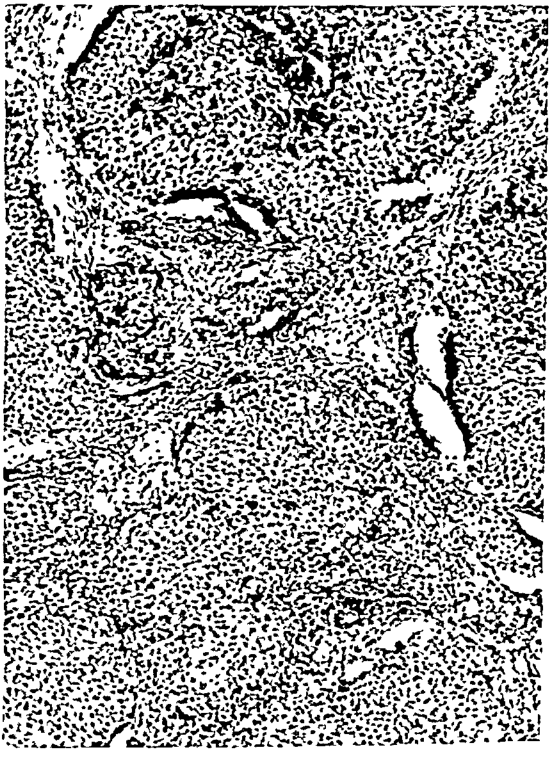

Fig 3. Squamous cell carcinoma (nonkeratinizing) of the prostate in case 7 (hematoxylin and eosin stain; ×80).

The origin of squamous cell carcinomas when localized to the prostate makes for interesting speculation. The polymorphism of epithelial cells was brought to attention in 1932.[5] These tumors can arise from 2 types of epithelium, namely, transitional epithelium of the prostatic urethra and metaplastic glandular epithelium of the prostate. Kahler said that the latter possibility was quite remote since squamous metaplasia (fig. 4) is relatively common while squamous carcinoma is uncommon. He found that 6 (3 per cent) of 195 carcinomas of the prostate were squamous cell carcinomas while squamousm etaplasia has been reported occurring in 15.9 per cent of benign prostates.[6] It is felt that the urethral epithelium is in most cases the origin in these tumors.

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[4] Gutierrez, Robert · Discussion. J. Urol , 61: 585, 1949.

[5] Broders, A. C : Carcinoma in situ contrasted with benign penetrating epithelium. J.A.M.A , 99: 1670–1674, 1932.

TABLE 1. *Primary squamous cell carcinoma of the prostate gland*

CASE	AGE, YRS.	DURATION OF SYMPTOMS	DIGITAL RECTAL FINDINGS*	CYSTOSCOPIC FINDINGS*	PATHOLOGIC FINDINGS*	IMMEDIATE RESULT OF TRANS-URETHRAL RESECTION	PERIOD OF SURVIVAL
1	59	6 mos.	Benign	Benign	Squamous cell carcinoma, grade 3 (keratinizing)	Good	3 mos.
2	52	4 mos.	Malignant	Ulcerating carcinoma	Squamous cell carcinoma, grade 3 (keratinizing)	Good	7 mos.
3	63	6 mos.	Benign	Malignant	Squamous cell carcinoma, grade 1	Good	11 mos.
4	53	1 mo.	Benign	Benign	Squamous cell carcinoma, grade 2 (keratinizing)	Good	3 mos.
5	62	3 mos.	Malignant	Benign	Squamous cell carcinoma, grade 3	†	10 mos.
6	65	2 yrs.	Benign	Benign	Squamous cell carcinoma, grade 3 (keratinizing)	Fair	6 yrs.
7	70	10 yrs.	Benign	Malignant	Squamous cell carcinoma, grade 3	Good	13 mos.

* Pertaining to prostate gland.
† Operation consisted of removal of specimen for microscopic examination.

SQUAMOUS CELL CARCINOMA OF THE PROSTATE GLAND ARISING AT THE VESICAL NECK

Eight cases in which a squamous cell carcinoma of the prostate arose primarily at the vesical neck have been observed at the clinic. The clinical and pathologic data in these cases are included in table 2. Histologically, the tumors in these cases could not be distinguished from those which arose primarily in the prostate gland. The only reason for placing them in a separate category is the difference in their point of origin. The operating surgeons expressed the opinion that these tumors arose at the region of the internal sphincter, either from the vesical or urethral mucosa. In each case, the tumor involved the prostate, and the examiner expressed the opinion that the prognosis was poor.

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[6] Sutton, E. B and McDonald, J. R.: Metaplasia of the prostatic epithelium: a lesion sometimes mistaken for carcinoma. Am. J. Clin. Path., **13:** 607–615, 1943.

In 4 of the 8 cases, rectal palpation did not disclose any evidence of a malignant tumor of the prostate. The grade of malignancy of the tumor was high in 7 of the 8 cases.

In 1 case (case 11), *roentgenographic examination* disclosed evidence of metastasis. The concentration of acid phosphatase in the serum was normal in this case. Unfortunately, the concentration of this enzyme in the serum was determined in only one other case. It also was found to be normal in this case.

CARCINOMA OF THE PROSTATE SECONDARY TO CARCINOMA OF THE RECTUM

In 6 cases of carcinoma of the prostate which have been observed at the clinic, the tumor arose primarily in the rectum and involved the prostate secondarily. In each of these cases, the tumor of the prostate caused obstructive symptoms that were severe enough to warrant transurethral resection. The malignant lesion of the rectum did not extend directly to the prostate in any of these cases; instead, the tumor of the prostate appeared to arise after involvement of the lymph nodes in the rectal shelf. In each of these cases, sections of the rectal lesion and the prostatic lesion were compared, and the 2 lesions were found to be identical (fig. 5 *a* and *b*).

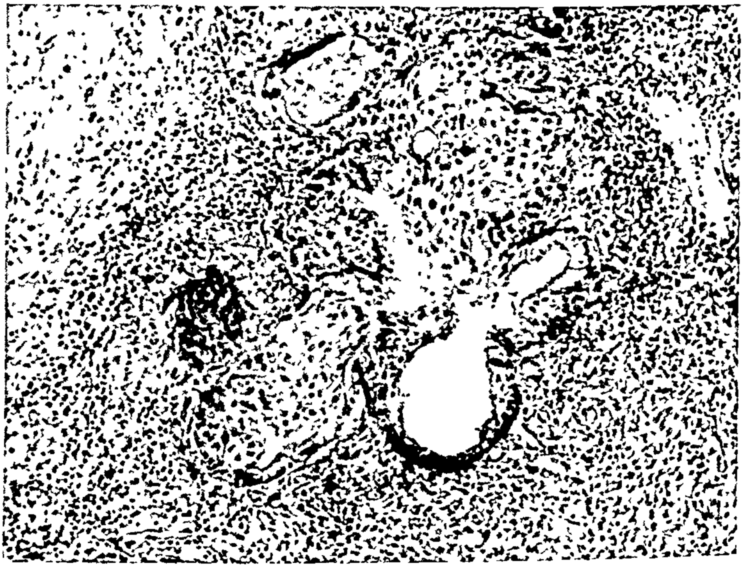
FIG 4 Benign squamous cell metaplasia in case 6 (hematoxylin and eosin stain; X95).

Although it is believed that Denonvilliers' fascia offers some barrier to the extension of carcinoma of the rectum into the prostate, such extension probably occurs more often than is realized. In 1943, Oppenheimer[7] reported several cases in which a carcinoma of the rectum or rectosigmoid extended to the prostate. Infiltration into the external sphincter was common in the 6 cases observed at the clinic, and we believe that it accounted for the incontinence in the cases in which this symptom was present. From six to fifty-three months elapsed before the carcinoma initially present in the bowel was recognized clinically to have extended to the prostate gland. It also seems significant that in the majority of cases the grade of malignancy of the primary lesion in the bowel was high, and that in 5 of the 6 cases the survival period was comparatively short after intestinal resection. In any case in which a carcinoma of the rectum has extended to the prostate gland, the prognosis is extremely poor.

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[7] Oppenheimer, G D. Late invasion of bladder and prostate in cancer of the rectum or rectosigmoid following abdomino-perineal resection Ann. Surg., 117: 456–467, 1943.

TABLE 2. *Secondary squamous cell carcinoma of the prostate gland arising primarily in the region of the vesical neck*

CASE	AGE, YRS.	DURATION OF SYMPTOMS	DIGITAL RECTAL FINDINGS*	CYSTOSCOPIC FINDINGS	PATHOLOGIC FINDINGS*	IMMEDIATE RESULT OF TRANSURETHRAL RESECTION	PERIOD OF SURVIVAL
8	57	Stricture for 30 yrs.	Benign	Cystitis; incrustation of vesical neck	Squamous cell carcinoma, grade 3 (keratinizing)	Good	14 mos.
9	58	4 mos.	Malignant	Contraction of vesical neck	Squamous cell carcinoma, grade 3	Good	5 mos.
10	62	2 yrs.	Malignant	Contraction of vesical neck	Squamous cell carcinoma, grade 3	Good	3 mos.
11	56	5 mos.	Malignant	Contraction of vesical neck	Squamous cell carcinoma, grade 3 (keratinizing)	Good	8 mos.
12	52	1.5 yrs.	Benign	Contraction of vesical neck	Squamous cell carcinoma, grade 3	Good	13 mos.
13	74	6 mos.	Benign	Malignant*	Squamous cell carcinoma, grade 3	Fair	8 mos.
14	67	2 yrs.	Benign	Malignant*	Squamous cell carcinoma, grade 2	Fair	6 mos.
15	44	1 yr.	Malignant	Malignant*	Squamous cell carcinoma, grade 3 (keratinizing)	Good	1 yr.

* Pertaining to prostate gland.

CARCINOMA OF THE PROSTATE SECONDARY TO CARCINOMA OF THE STOMACH

We shall report a case in which a carcinoma of the stomach extended to the prostate gland. We are not aware of a similar case that has been reported in the literature.

Case 22.—A man, aged 47 years, came to the clinic on October 1, 1928, and was found to have a carcinoma of the stomach. At that time, digital examination of the rectum did not disclose any abnormality of the prostate. A posterior Polya partial gastrectomy was performed, and the pathologist reported that

TABLE 3. *Secondary carcinoma of the prostate gland arising primarily in the rectum*

CASE	AGE, YRS.	DURATION OF URINARY SYMPTOMS*	DIGITAL RECTAL FINDINGS†	CYSTOSCOPIC FINDINGS†	INTERVAL BETWEEN RECTAL OPERATION AND TRANSURETHRAL RESECTION	PATHOLOGIC DIAGNOSIS		PERIOD OF SURVIVAL‡
						Rectal lesion	Prostatic lesion	
16	39	1 mo.	Hard, gritty mass	Extreme fixation of vesical neck	5 mos.	Adenocarcinoma; grade 4 (Broders') type C (Duke's)	Adenocarcinoma; grade 4 (Broders'); type C (Duke's)	8 mos.
17	59	5 mos.	Small and benign	Fixation of vesical neck	2.5 yrs.	Adenocarcinoma; grade 4 (Broders'); type C (Duke's)	Colloid adenocarcinoma; grade 4 (Broders')	4 mos
18	62	3 mos.	Small and firm	Malignant fixation	17 mos.	Adenocarcinoma; grade 2 (Broders'); type C (Duke's)	Adenocarcinoma; grade 2 (Broders'); type C (Duke's)	18 mos.
19	62	8 mos.	Large mass	Fixation of vesical neck	7 mos.	Adenocarcinoma; grade 3 (Broders'); type C (Duke's)	Adenocarcinoma; grade 3 (Broders'); type C (Duke's)	11 mos.
20	58	2 mos.	Small and benign	Benign	1.5 yrs.	Adenocarcinoma; grade 2 (Broders'); type B (Duke's)	Adenocarcinoma; grade 2 (Broders'); type C (Duke's)	10 mos.
21	35	1 mo.	Benign	Fixation of vesical neck	4.5 yrs.	Adenocarcinoma; grade 3 (Broders'); type C (Duke's)	Adenocarcinoma; grade 3 (Broders'); type C (Duke's)	6 mos.

* Prior to transurethral resection.
† Pertaining to prostate gland.
‡ After transurethral resection.

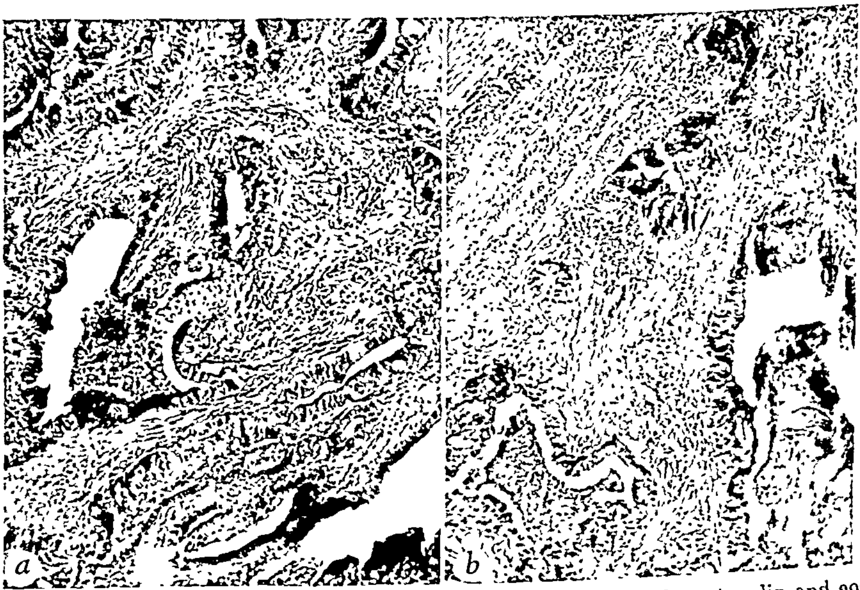

FIG. 5. *a*, Adenocarcinoma, grade 3, of the rectum in case 21 (hematoxylin and eosin stain; ×80); *b*, adenocarcinoma, grade 3, of prostate in case 21 (hematoxylin and eosin stain; ×80).

the lesion was a carcinoma, grade 4, of the pylorus which had perforated into the gastrocolic omentum and involved the lymph nodes.

After the operation, the patient's health remained satisfactory until 1931, when symptoms of urinary obstruction and some urinary incontinence developed. When he returned to the clinic on April 27, 1932, his bladder was found to contain 500 cc of residual urine. Examination did not disclose any evidence of a recurrence of the carcinoma in the upper part of the abdomen, but the presence of a malignant lesion of the pelvis was suspected. The prostate gland was enlarged and very firm in consistency. On May 4, 1932, a transurethral resection was performed, and a total of 9 gm. of prostatic tissue was removed. The pathologist who examined the surgical specimen reported that the lesion was a colloid carcinoma (fig. 6 *a* and *b*) which likely was secondary to the carcinoma of the stomach. The sections of the gastric and prostatic lesions recently were examined by one of us (Broders), and the 2 lesions were found to be identical.

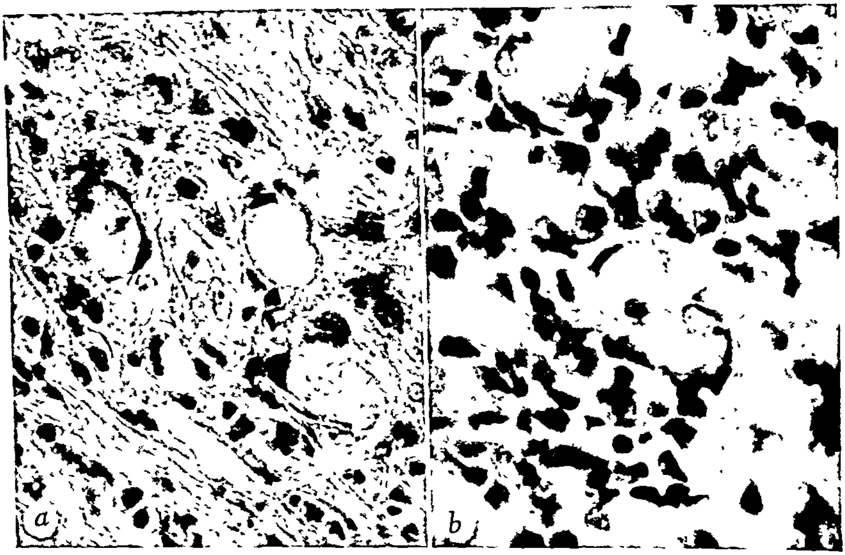

FIG. 6. *a*, Adenocarcinoma, grade 4, of stomach in case 22 (hematoxylin and eosin stain; ×600); *b*, adenocarcinoma of prostate in case 22 (hematoxylin and eosin stain; ×600).

The urinary symptoms were relieved, and the patient continued to work until the spring of 1933, when his health began to fail rapidly. Ankle edema developed, and it became evident that the carcinoma of the stomach had recurred and metastasized to the thorax. The patient died at his home on April 14, 1933. A necropsy was not performed.

AN UNUSUAL MUCOID CARCINOMA APPARENTLY ARISING PRIMARILY IN THE PROSTATE GLAND

We also shall report a case in which an unusual mucoid carcinoma apparently arose primarily in the prostate gland. In 1928, Klissurow[8] reported a case of gelatinous carcinoma of the prostate gland. The tumor in his case evidently was similar to the one in the case which we shall report.

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[8] Klissurow, A.: Ein Fall von Carcinoma gelatinosum Prostatae. Virch. Arch. f. path. Anat., 268: 515–523, 1928.

Case 23.—A man, aged 65 years, returned to the clinic in November 1948, because of progressive urinary obstruction which had been present for a long time. Subtotal thyroidectomy had been performed for exophthalmic goiter in 1942, suppurative disease of the lung had developed in 1942, and lower and middle lobectomy of his right lung had been performed for squamous cell carcinoma, grade 3, in 1946.

Physical examination and laboratory tests did not disclose any evidence of recurrence of the carcinoma of the lung. The concentration of urea was 22 mg. per 100 cc of blood. The values for the alkaline and acid phosphatase were 3.6 and 0.7 King-Armstrong units, respectively, per 100 cc of serum. Urinalysis disclosed pyuria, grade 3, but a roentgenogram of the kidneys, ureters and bladder did not reveal any abnormality. His prostate gland was enlarged, moderately irregular, and hard. Proctoscopy, which was performed because of the presence of mild constipation, revealed a small polyp 12 cm. above the anal margin. The polyp was fulgurated.

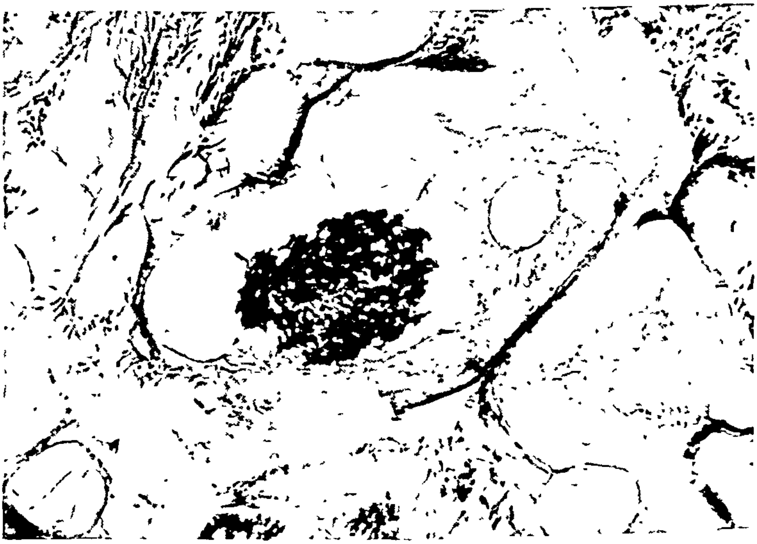

FIG. 7. Mucoid adenocarcinoma of prostate in case 23 (hematoxylin and eosin stain; ×85).

Cystoscopy disclosed an avascular prostatic tumor which was fungating and necrotic in character and extended into the vesical cavity for a distance of 1½ inches (3.8 cm.). The tumor was removed by transurethral resection. A total of 71 gm. of tissue was removed in the course of the operation, and the vesical neck was opened widely. Microscopic examination of the surgical specimen revealed that the tumor was a mucoid adenocarcinoma, grade 2 (fig. 7).

The functional result of the operation was good, but the prognosis was considered poor. A squamous cell epithelioma, grade 1, of the patient's lip was excised in December 1948. The patient died at his home on July 1, 1949.

SUMMARY

This report is based on a review of 7 cases in which a squamous cell carcinoma apparently was confined to the prostate gland, 8 cases in which a squamous cell carcinoma arose in the epithelium of the vesical neck and involved the prostate gland, 6 cases in which an adenocarcinoma of the rectum subsequently extended to the prostate gland, 1 case in which metastasis to the prostate gland occurred several years after operation for carcinoma of the stomach, and 1 case in which a mucoid carcinoma of the prostate gland developed after the removal of a carcinoma of the lung.

In the majority of cases, the smooth, soft consistency of the prostate gland led the examiner to believe that a malignant lesion was not present.

After the diagnosis of a malignant lesion was made, hormonal therapy was found ineffective in these cases. There was no elevation of the value of the serum acid phosphatase in those cases in which the concentration of this enzyme was determined.

The survival period following operation was comparatively short. It was much shorter than it usually has been in the cases of adenocarcinoma of the prostate which we have observed.

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SERUM ALDOLASE AND ITS RELATIONSHIP TO THE HORMONAL CONTROL OF CANCER

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To consider cancer from the biochemical point of view, there are certain distinguishing metabolic characteristics between the malignant and the normal cell that obtain regardless of histological appearance.[1] Warburg[2] established that human and rat cancer tissue possess a high rate of anaerobic and aerobic glycolysis. Dickens and Simer[3] demonstrated further that tumors have a respiratory quotient of only 0.85 instead of 1.0 when incubated aerobically with glucose. This fact is in contradistinction to certain normal tissues such as brain, retina and the embryo, having high anaerobic glycolysis. In 1943 Warburg and Christian[4] reported that five of the enzymes involved in glycolysis were present normally in the serum of rats. The serum concentration of two of these enzymes, aldolase and triose isomerase, were increased above normal in tumor-bearing rats. These results were confirmed and extended by Sibley and Lehninger.[5] It was concluded that increased serum aldolase concentration in tumor-bearing rats was apparent however only when the tumor weight exceeded two to three per cent of total body weight. In addition, as significant elevation of serum aldolase occurred in only 20 per cent of cases of human cancer tested, the levels of serum aldolase in the human were not of general diagnostic usefulness.

The fact remains that a high rate of glycolysis is a general biochemical characteristic of malignant cells. One of the enzymes of the glycolytic mechanism, aldolase, appears in large amounts in the serum of tumor-bearing rats and in certain patients with cancer. Benign tumors and pregnancy do not result in elevated serum aldolase levels. The explanation and significance of why serum aldolase should appear in large amounts in the serum of any patient with cancer is unknown. The effect of increased or decreased cancer activity on serum aldolase concentration has not been studied. The influence of the endocrine system on regulation of serum aldolase levels has not been reported.

The hormonal control of specific types of cancer is recognized. Certain of the leukemias undergo remission by administration of ACTH or cortisone. Patients with advanced breast cancer may have remission of the disease by use of testosterone or estrogen. Huggins[6] has demonstrated the prolonged remission possible

This investigation was aided by an American Cancer Society Institutional Grant.
Accepted for publication June 6, 1952.

[1] Greenstein, J. P.: Properties of Tumors. Biochemistry of Cancer. New York: Academic Press, 1947, pp. 175–315.

[2] Warburg, O. Über den Stoffwechsel der Tumoren. Berlin: Springer, 1926.

[3] Dickens, F. and F. Siner. CXLIII. The metabolism of normal and tumor tissue. II. The respiratory quotient and the relationship of respiration to glycolysis. Biochem. J., **24:** 1301, 1930.

[4] Warburg, O. and W. Christian: Gärungsfermente in Blutserum von Tumor-Ratten. Biochem. Ztschr., **314:** 399, 1943.

[5] Sibley, J. A. and A. L. Lehninger. Aldolase in the serum and tissues of tumor-bearing animals. J. Nat. Cancer Institute, **9:** 303, 1949.

[6] Huggins, C. and Hodges, C. V.: Studies on prostatic cancer. I. The effect of castration,

with metastatic cancer of the prostate by orchiectomy, estrogen therapy and adrenalectomy.

This paper presents the effect of hormonal therapy on serum aldolase in a series of patients with prostatic cancer.

METHODS

1) A group of patients with untreated, advanced, prostatic cancer were studied. Serum aldolase concentrations were determined prior to and during therapy. Treatment consisted of orchiectomy or the daily intramuscular administration of 5 mg. of diethylstilbestrol. Two patients had bilateral adrenalectomy for advanced prostatic cancer.

2) The function of aldolase in the glycolytic mechanism of intracellular metabolism is established precisely due to its high degree of substrate specificity. Aldolase catalyzes the reversible cleavage of fructose-1,6-diphosphate to one mole each of glyceraldehyde phosphate and dihydroxyacetone phosphate. Serum aldolase was determined by the colorimetric method of Sibley and Lehninger.[7] This procedure depends essentially on measuring activity of aldolase per ml. of human serum by its capacity to catalyze the breakdown of hexose diphosphate (HDP). The triose end products are determined colorimetrically by the addition of 2,4-dinitrophenylhydrazine in the presence of alkali. As serum usually contains triose phosphate isomerase which rapidly converts the glyceraldehyde phosphate to dihydroxyaceone phosphate, the reaction is stabilized by the addition of hydrazine. Due to the hydrogen ion concentration and buffering activity of the blood it was not necessary to use tris buffer in serum aldolase determinations.

This method for determination of aldolase is a practical procedure and the results obtained are significant for relative alterations in serum concentrations. The method presents certain pitfalls for the determination of absolute quantities of aldolase. Crystalline rabbit aldolase was extracted and recrystallized according to the procedure of Cori.[8] Recovery of a known amount of aldolase by the method of Sibley and Lehninger was frequently in error to a magnitude of 15 per cent. On occasion serum aldolase determinations failed to reveal any of the enzyme present, while duplicate determinations of the same sample demonstrated the expected presence of a normal quantity of aldolase. The explanation for this peculiarity is unknown. As a consequence duplicate, and often quadruplicate, determinations were performed on each sample of serum or tissue.

3) Serial enzyme levels were obtained on all humans, dogs and rabbits in the experiment. It was necessary therefore to compare fluctuations in enzyme level with some other constituent of the serum. Variations in aldolase concentration per ml. of serum could conceivably be explained solely by alterations in total

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of estrogen and of androgen injections on serum phosphases in metastatic carcinoma of the prostate. Cancer Research, 1: 293, 1941.

[7] Sibley, J. A. and Lehninger, A. L.: Determination of aldolase in animal tissues. J. Biol. Chem., 177: 859, 1949.

[8] Taylor, J. F., Green, A. H. and Cori, G. T.: Crystalline aldolase. J. Biol. Chem., 173: 591, 1948.

blood volume due to blood loss, hemodilution from intravenous fluids or hemoconcentration due to dehydration. Serum aldolase values per ml. were compared with total protein concentration per 100 ml. in the form of an Aldolase Index.

$$\frac{\text{Serum aldolase units 1 ml.}}{\text{Total protein G/100 ml.}} = \text{Aldolase Index}$$

Clinically, it was seldom necessary to express aldolase as an index. To the contrary in dogs, and particularly serial serum analyses in rabbits, frequent use of an aldolase index was required to obtain significant results.

All aldolase values are expressed as units which equal c. mm. of HDP split at 38°C per hour. Units may be converted to micromoles by dividing by 22.4. The range of normal for human serum aldolase is 2.0–9.6 with a mean of 5.8 units.

4) All phosphatase units are those of King and Armstrong.[9] Total protein was determined by the micro-Kjeldahl method of Ma and Zuazaga.[10]

RESULTS

Sixteen consecutive, proven, unselected and untreated patients with advanced cancer of the prostate were studied. Prior to treatment the serum aldolase was elevated above normal in 12 of these patients. Following orchiectomy or estrogen therapy the elevated serum aldolase concentration returned to normal range in 10 of the 12 patients (fig. 1).

Two of the 4 patients who failed to demonstrate a pretreatment increased serum aldolase had normal serum acid phosphatase values despite the presence of extensive metastases. No clinical improvement resulted from hormonal therapy in two of these 4 patients as judged by persistence of back pain and symptoms of obstructive prostatism, anorexia and radiographic observation of metastases. Although these 4 cases had no elevation of serum aldolase concentration, following orchiectomy or estrogen therapy the concentration of serum aldolase was greatly reduced on repeated determinations in 2 patients (fig. 2).

Breakdown of data obtained from the 12 patients who had elevated serum aldolase prior to treatment reveals 2 patients who had normal serum acid phosphatases (fig. 3) and one additional patient with both acid and alkaline phosphatase values within normal range. Following hormonal therapy this last patient failed to demonstrate any clinical evidence of cancer deactivation. The aldolase concentration paralleled this clinical course and remained above 15 units. The remaining patient that failed to demonstrate a return to normal range of serum aldolase following therapy had an excellent clinical and biochemical (phosphatase) remission of his cancer.

Following orchiectomy or estrogen therapy, patients with advanced prostatic cancer that experience a remission of their disease characterized by return to

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[9] King, E. J. and Armstrong, A. R.: Canad. M.A.J., **31:** 376, 1934.

[10] Ma, T. S. and Zuazaga, G.: Micro-Kieldohl determination of nitrogen. A new indicator and improved rapid method. Industrial and Engineering Chemistry (Analytical Edition), **14:** 280, 1942.

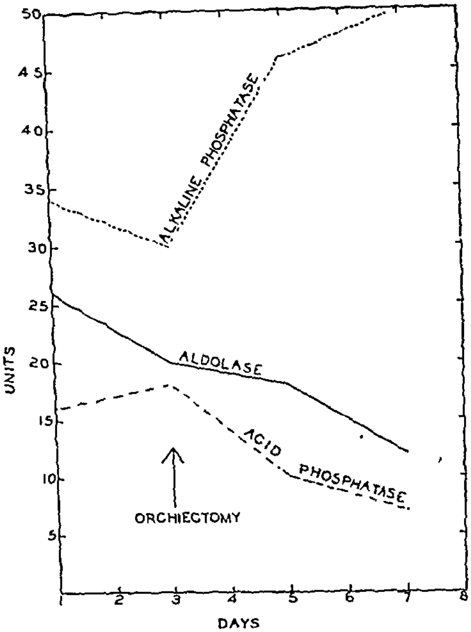


FIG. 1 Patient with metastatic prostatic cancer demonstrating increased serum concentrations of aldolase and also acid and alkaline phosphatase. Orchiectomy resulted in deactivation of cancer activity biochemically and clinically. Aldolase and acid phosphatase decreased toward normal. Phosphatase values expressed as King Armstrong units.

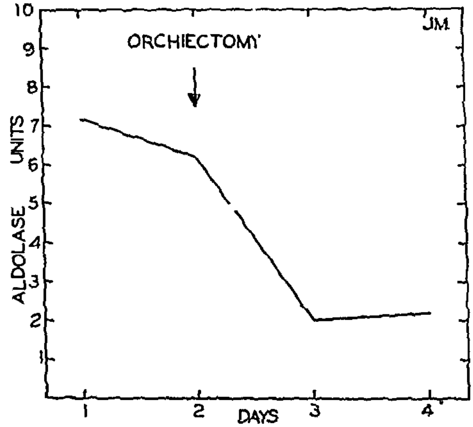


FIG. 2 *Patient with advanced* prostatic cancer treated by androgen withdrawal. Although preoperative serum aldolase levels *were not above normal* range, observe marked decrease following orchiectomy. Serum acid phosphatase concentration was *normal*.

normal of serum acid and alkaline phosphatases, seldom *demonstrate* a second elevation of serum acid phosphatase with subsequent exacerbation in activity of the malignancy. Although these same patients *may terminally* demonstrate an elevation of alkaline phosphatase, the serum acid phosphatase usually remains nearly normal. Serum aldolase has been determined on three such patients and invariably has been markedly elevated in the presence of normal acid phosphatase.

Two patients had bilateral adrenalectomy for prostatic cancer. The aldolase concentrations were two to three times normal preoperatively. Administration of cortisone, 100 mg. twice daily, prior to surgery did not alter the enzyme level. Following adrenalectomy the aldolase decreased nearly to normal range in both patients (fig. 4).

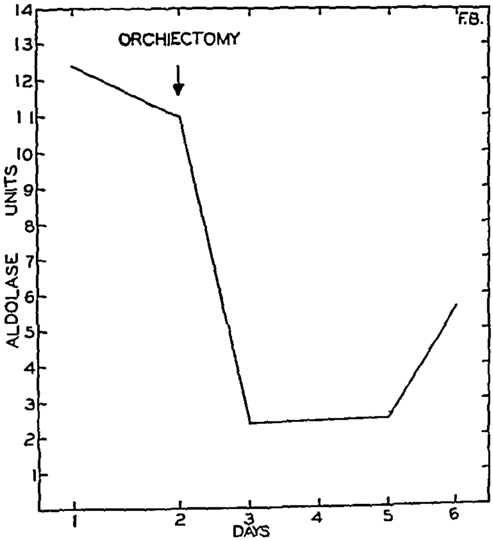


FIG. 3. Despite presence of extensive metastases from prostatic cancer, patient failed to demonstrate elevation of acid phosphatase. Increased preoperative serum aldolase concentration may be compared with normal levels following orchiectomy.

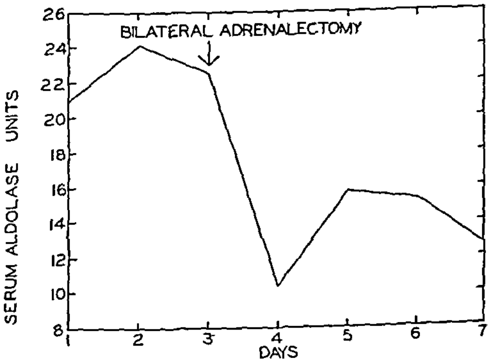


FIG. 4. Effect of bilateral adrenalectomy on activity of prostatic cancer. Observe that despite marked decrease in concentration following surgery, serum aldolase remains elevated above normal range. Serum acid phosphatase values were normal before and after surgery.

CONTROL EXPERIMENTS

To determine whether the observed reduction in quantity of serum aldolase following orchiectomy, adrenalectomy or estrogen therapy was produced by the endocrine imbalance effected or by remission of cancer activity, 3 patients with advanced bronchiogenic carcinoma were studied. Two of the patients had increased serum concentrations of aldolase. Following orchiectomy the clinical condition of the patients deteriorated or was unimproved. In either situation, aldolase increased markedly in the serum (fig. 5). It would appear that in these cancer patients androgen withdrawal has no effect on serum aldolase concentration.

Additional studies were performed on an impotent 25 year old man with atrophic testes. There was no constant variation from normal of serum aldolase levels either before or after institution of a three-week-course of intramuscular testosterone proprionate, 25 mg. daily.

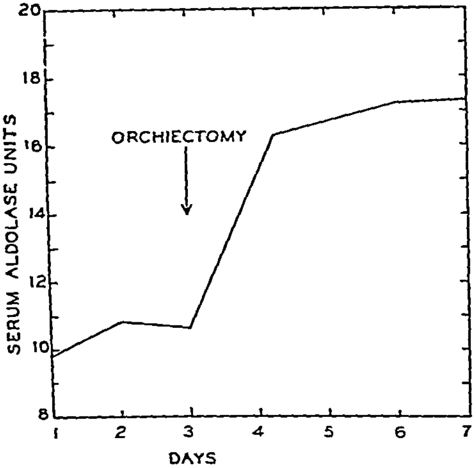


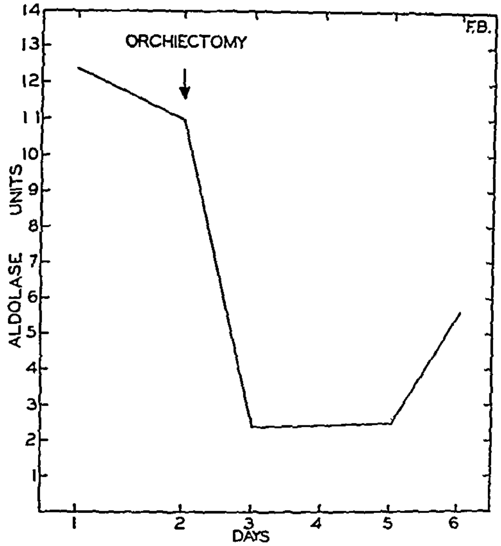
FIG. 5. Patient with bronchiogenic carcinoma. No clinical improvement following androgen withdrawal. Effect is identified biochemically by elevation of serum aldolase concentration.

Orchiectomy was performed next on 4 dogs. Two additional dogs were given a 5 mg. daily, intramuscular, injection of stilbestrol. No statistically significant alteration in serum aldolase concentration was observed.

The effect of anesthesia, operation, and blood loss on the quantity of circulating aldolase was investigated in humans. Five major operative procedures were performed for nonmalignant lesions, such as nephrectomy for hydronephrosis, pyeloplasty for ureteropelvic obstruction and suprapubic prostatectomy for benign prostatic hypertrophy. There was no significant alteration in serum aldolase index observed following any of the procedures providing hydration was not altered. The same result was obtained following sham operation on three dogs using intravenous nembutal anesthesia. Two dogs were starved for 1 week and 2 dogs were dehydrated for 10 days. No significant increase or decrease in the concentration of serum aldolase index was observed.

The greatest increase in aldolase concentration was observed in those patients with far advanced prostatic cancer having marked loss of weight. It was necessary to determine therefore the relationship between nitrogen balance and serum aldolase level. Results obtained indicate that it is possible for a patient to be in nearly normal. Serum aldolase has been determined on three such patients and invariably has been markedly elevated in the presence of normal acid phosphatase.

Two patients had bilateral adrenalectomy for prostatic cancer. The aldolase concentrations were two to three times normal preoperatively. Administration of cortisone, 100 mg. twice daily, prior to surgery did not alter the enzyme level. Following adrenalectomy the aldolase decreased nearly to normal range in both patients (fig. 4).



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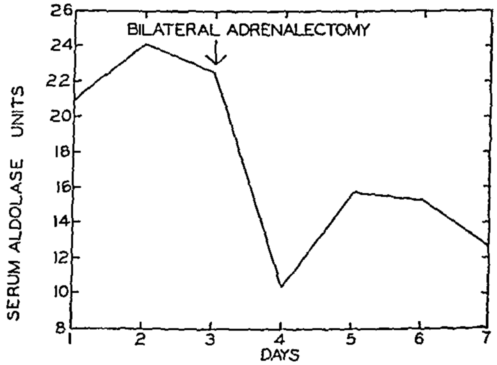

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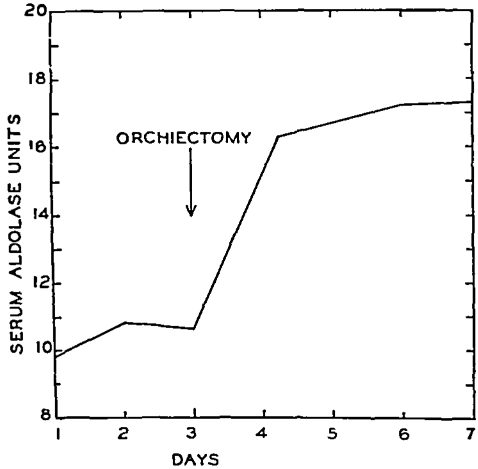

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The greatest increase in aldolase concentration was observed in those patients with far advanced prostatic cancer having marked loss of weight. It was necessary to determine therefore the relationship between nitrogen balance and serum aldolase level. Results obtained indicate that it is possible for a patient to be in either negative or positive nitrogen balance and have a co-existent increased serum aldolase. Conversely, a normal serum aldolase level may be observed in a patient in negative nitrogen balance. The concentration of serum aldolase is apparently independent of the state of nutrition. The results of this investigation are to be published in detail elsewhere.

The sera of 21 patients with benign hypertrophy of the prostate were examined for serum aldolase and all were within normal range.

DISCUSSION

Twelve of 16 patients with advanced untreated prostatic cancer had elevation of serum aldolase levels. Following hormonal therapy the aldolase concentration returned to normal in 10 of the 12 patients studied.

It has not as yet been explained why one of the enzymes involved in tumor metabolism should appear in large amounts in the serum of certain patients with cancer. It has been demonstrated however that with remission of prostatic cancer activity there is a return to normal of serum concentration of this enzyme. In those patients where hormonal therapy is ineffectual in producing deactivation of the cancer, serum aldolase remains increased above normal range.

Increased concentrations of serum acid phosphatase are generally considered specific for advanced prostatic cancer, although it is not elevated in all patients with this disease. Prior to any therapy, patients with metastatic cancer of the prostate were studied that had normal serum acid phosphatase and markedly increased serum aldolase. It would appear therefore that serum aldolase concentration is independent of acid phosphatase. This impression is strengthened by observations on 3 patients refractive to hormonal therapy dying of prostatic cancer. None had increased acid phosphatase determinations, while all had large amounts of aldolase in the serum.

Data obtained from control experiments indicate that the return to normal of elevated serum aldolase following orchiectomy, estrogen administration or adrenalectomy is not an endocrine effect, but rather a measure of cancer activity. Patients with bronchogenic carcinoma have no clinical improvement from orchiectomy. Serial serum aldolase determinations in these patients demonstrate the same lack of beneficial effect. An impotent patient with atrophic testes failed to elicit any fluctuation in aldolase concentration following testosterone therapy. Orchiectomy or estrogen administration in normal dogs did not alter serum aldolase levels. Those patients with prostatic cancer that experience no remission from androgen withdrawal, usually fail to have alteration in aldolase concentration.

The effect of anesthesia, surgery, blood loss and state of nutrition has been investigated and is found to be independent of serum aldolase concentration.

SUMMARY

A new modality is presented for determination of the activity of prostatic cancer by measurement of serum aldolase. The increased aldolase concentration usually returns to normal range following hormonal therapy if cancer deactivation is produced. This effect is apparently independent of serum acid phosphatase, the endocrine system, surgery or nutritional status of the patient.

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VAGINAL URINARY STONE

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The occurrence of urinary calculi in the vagina is quite rare. There have been a number of causes for the formation of calculi from whatever source in the vagina; these include: stagnation of menstrual flow, vaginal cysts, calcified fibroids, calcifications of mucus cells, and urinary leakage into the vagina. The older literature records more causes of this condition than the most recent, probably due to the fact that colpoclysis formerly was done more frequently than at the present time. Less than 30 cases of vaginal concretions from whatever cause have been reported and probably less than half of these have been due to the urinary factor.

CASE REPORT

J. A. (CMH No. 77986) a 6 year old girl was first seen on April 24, 1951. The mother gave a history of intermittent and unconscious emptying of the bladder ever since birth. The child had been operated on at the age of 3 days for some type of spinal condition. She also stated that the child had partial incontinence of feces and was unable to walk naturally. A brief examination disclosed a screaming child with a mild hydrocephalus and with atrophy of the muscles innervated by the sacral segments and with a marked excoriation and ulceration of the labia and vagina. A large stone was seen to present at what was first thought to be a vaginal orifice, but after further inspection, as well as could be carried out under the circumstances, it was decided that a large stone was present in a paralyzed bladder which had dilated the bladder neck and was presenting at the external meatus. An x-ray (fig. 1) was made and without further ado, the child was referred for admission to the Cabarrus Memorial Hospital. After admission, a better history was obtained and the old hospital records were examined. The child had been born on April 21, 1945 and was delivered in the home by a midwife. At the age of 3 days, the child was admitted to the Cabarrus Memorial Hospital with chills and fever due to an infected meningocele and spina bifida. On May 8, 1945, after preoperative preparation with hot soaks and antibiotics to limit an infection present, the child was operated on by Dr. W. R. Floyd of Concord, N. C. A subcutaneous and cutaneous abscess was incised; the meningocele could not be closed; no definite nerve elements were identified at surgery nor found on pathological examination. The infant was discharged on May 15, 1945; there was one note stating that the child was voiding normally at the time of discharge, and there were no signs of hydrocephalus. The wound had healed by secondary intention but without infection.

From this time on, the child developed almost normally but with an associated mild hydrocephalus. She had the usual childhood diseases but had been almost free from other infections. The child had learned to walk at a normal age although there was much difficulty in learning balance. She walked with a foot drop but did learn to run and play with other children. Bowel and bladder incontinence had always been present and marked urinary incontinence developed when any stress was present. For 2 years before admission to the hospital the child dribbled urine almost constantly day and night and with a gush of urine on every movement. The genitalia were so raw that the child could not walk, sit or lie with comfort for several weeks prior to admission.

Physical examination: The child was alert and intelligent but did not desire to co-operate in any way. The head showed a definite but mild hydrocephalus. The throat showed hypertrophied tonsils and some irritation. The abdominal examination was normal and there was normal muscular strength throughout. On exposing the genitalia, the labia majora was markedly hypertrophied with many ulcers along the apposing surfaces. Numerous so-called "kissing ulcers" were found. No urethral orifice could be determined; there was a white, glistening, smooth stone presenting through what appeared to be either the vagina or the ureteral orifice. On as careful examination as could be done under the circumstances, it was thought that the stone presented through a relaxed vesical outlet and that the vagina could not be palpated due to being displaced by the mass of the stone. The stone could be grasped and moved with forceps and could be felt with the tip of the examining finger. There were hyperactive reflexes at the knees; the remainder of the peripheral reflexes in the legs were absent. There was bilateral foot drop and atrophy of the muscles innervated by the sacral dermatomes.

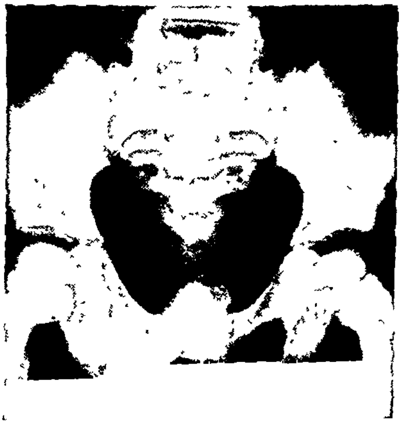

FIG. 1. Plain urogram shows large vaginal calculus. Spina bifida also demonstrated.

Urinalysis showed reaction of 7.5 and 1 to 2 pus cells per high powered field. Blood count: 3,440,000 red cells; 66 per cent hemoglobin; 12,100 white count with a slight left shift. Excretory urography showed an entirely normal upper tract, the only abnormality being demonstrated by the calculus in the x-ray (fig. 1).

The preoperative diagnosis was atonic myogenic bladder with vesical calculus. Cystolithotomy and cystostomy were planned with a fascial sling operation for incontinence at a later date when the bladder capacity was increased and the vaginal tissue had returned to normal.

On April 26, 1951, under drop ether anesthesia, a suprapubic cystostomy was performed and showed a normal but contracted bladder with no stones. The stone could be felt below and through the bladder wall. Next the vagina was exposed, a mediolateral episiotomy was done, and a large stone was broken first with a Kocher clamp, and then extracted from the vagina. The vagina was irrigated and inspected carefully and found to be normal except for enlargement due to the stone. The bladder was then filled and no urine could be seen to leak into the vagina from the bladder.

On May 4, 1951, cystoscopy was done. The urethra was very small and difficult to locate. It was in the usual position and a marked meatal stricture was present, the urethral meatus being represented by just a small dimple. A No. 6 ureteral catheter only could be passed into the bladder. Careful dilatation of the urethra was done so that a No. 11 McCarthy cystoscope could be introduced. No abnormality was seen in the bladder except the contracture as noted at the time of cystostomy. Another inspection of the vagina revealed no communication of the vagina with the bladder or urethra.

The child made a satisfactory recovery. She is now socially acceptable by her little friends and they do not tease her any more for smelling like urine. She is making a good adjustment in school and it is planned in the future to do a fascial sling operation around the urethra to give continence to the bladder. In the meantime, she is under hydraulic distention of the bladder which is gradually increasing in capacity.

SUMMARY

A case of vaginal urinary stone has been presented. The correct diagnosis was suspected at first examination but this observer could not believe this possibility and therefore an erroneus diagnosis was made.

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TORSION OF THE APPENDIX EPIDIDYMIS AND APPENDIX TESTIS: THREE CASE REPORTS

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The purpose of this paper is to present three additional cases of torsion of the appendices of the testicle and epididymis.

INCIDENCE

Torsion of the vestigial structures about the superior pole of the testis and the epididymis has been reported infrequently. Seidel and Yeaw reviewed the literature in 1950 and reported 8 cases of their own which brought the total reported to 107 cases. This condition is probably not so rare as the number of reported cases would seem to indicate. It has been reported to occur bilaterally, in cryptorchidism, and Shattocks reported the only case of simultaneous torsion of two appendices of the same testis. In a 2-year period at Brooke Army Hospital, among 2,470 urologic admissions, 2 cases of torsion of the appendix epididymis and one of torsion of the appendix testis were seen, an incidence of one in 823 urologic admissions.

ANATOMY AND HISTOPATHOLOGY

The embryonic rudiments near the superior pole of the testis consist of: the appendix testis or hydatid of Morgagni, a remnant of the cranial end of the müllerian duct; the appendix epididymis or stalked hydatid derived from the cranial mesonephric tubules; the paradidymis or organ of Giraldes, a rudiment of the caudal mesonephric tubules; and the ductuli aberrantes of Haller, also derived from the caudal mesonephric tubules. As noted by Randall, any of these structures may undergo torsion. The cause of this torsion is unknown.

SYMPTOMATOLOGY

Symptoms usually consist of unilateral scrotal pain of sudden onset which is constant; occasionally lower abdominal pain may occur with no reference to the testicle. Early, temperature elevation is absent. The involved structure can be palpated and differentiated from the adjacent epididymis and testis. It will be markedly tender. Later, swelling will interfere with diagnosis by palpation, thus making it necessary to consider torsion of the spermatic cord, acute epididymitis, abscess of the epididymis and mumps orchitis in the differential diagnosis. If this condition is considered, differential diagnosis is not difficult. Many cases go unrecognized and have a long, painful course before resolution. With a definite diagnosis of torsion of the appendix testis or appendix epididymis, surgery is not essential since the symptoms will gradually subside. However,

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excision of the inflamed or gangrenous structure will shorten the period of morbidity. Though the condition is reported much more common in infants, two of the 3 cases presented below were in young adults.

HISTOPATHOLOGY

The microscopic anatomy of the appendix testis was studied by Vermeulen and Hagerty who pointed out that standard textbook descriptions of the structure were inaccurate. They found it to be a solid rather than a cystic structure, covered with columnar epithelium and containing loose connective tissue in which duct-like, ciliated epithelial inclusions are occasionally seen. The appendix epididymis is composed of cystic spaces lined by pseudo-palisaded columnar epithelium containing pale amorphous material, surrounded by a loose fibromuscular stroma and covered by mesothelium. There is nothing unusual about the ischemic necrosis of the appendices as a result of torsion.

CASE REPORTS

Case 1. A 1-year old white boy had a 3-day history of swelling and redness of the right side of the scrotum. Temperature was normal. Tenderness was minimal. A slight hydrocele formation precluded accurate palpation of the testicle and epididymis. Because torsion of the spermatic cord could not be ruled out, the scrotum was explored under open drop ether anesthesia. A gangrenous appendix epididymis which had undergone torsion and a 10 cc accumulation of inflammatory hydrocele fluid was found. The appendix epididymis was excised. The patient left the hospital after a 1-day stay and recovery was uneventful.

Case 2. A 32-year old white man was admitted with a 12-hour history of acute pain in the right testis following lifting a 15-pound weight. Temperature was normal. Examination revealed the superior pole of the right epididymis to be tender and swollen. Exploration was performed under intravenous pentothal anesthesia. Two epididymal appendices were found to be swollen and gangrenous and were excised. Recovery was uneventful.

Case 3. A 24-year old white man had sudden, constant right testicular pain on the eighth day after a right pyeloplasty. Temperature was normal. Eight hours after the onset of pain examination revealed a 10 by 7 by 7 mm. tender mass at the superior pole of the right testis but distinct from the epididymis and testis. The diagnosis of torsion of the appendix testis was made. Under local anesthesia the scrotum was opened over the mass and a gangrenous right appendix testis was found and removed.

SUMMARY

Two cases of torsion of the appendix epididymis and one of the appendix testis are reported, bringing the total reported cases to 110.

The second instance of simultaneous torsion of two appendices is recorded.

Surgical excision is the treatment of choice and may be performed under local anesthesia.

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A TRUE HERMAPHRODITE: CASE REPORT

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Hermaphroditism has captivated the curiosity of the layman and intrigued the physician for centuries. Until recent years many of these "misfits" were forced to live a carnival existence full of anguish and remorse.

The sociological and psychological implications of such cases are well demonstrated in Hugh Young's volume on this subject.[1] He reviewed 20 cases of true hermaphroditism, including one of his own. At a later date he added another case, thereby making a total of 21 cases reported up to 1937.

One of these cases was driven to suicide because "he" was not permitted to live a normal life. Today, however, with the advances of modern surgery and endocrinology, the hermaphrodite has a better chance of a normal happy life.

Quite often the surgeon is faced with a dilemma as to the solution of the intersex problem. However, a careful history with emphasis on the psychological and sociological aspects, together with estrogen-androgen activity of the urine will help decide which is the predominant sex and how it may be preserved and abetted.

A review of the literature reveals reports of approximately forty cases of true hermaphroditism which meet the pathological criteria.

A study of these 40 cases reveals many interesting facts. A true hermaphrodite is an individual who has the gonads and external genitalia of both sexes and is capable of living as either male or female. The etiology of this condition is unknown but there appears to be a strong familial tendency. The vast majority of reported cases have a hypospadias or some other abnormality of the external genitalia. Only two cases are reported with normal external genitalia.[2, 3] Approximately 90 per cent of these cases reveal an ovotestis. Two cases have been reported with no ovotestes. One of these was capable of secreting sperm and ova simultaneously, with monthly bloody urethral discharge.[2] Theoretically, self impregnation would be possible but this has never been reported.

The case we wish to present is unusual since no momentous surgical decision was necessary.

CASE REPORT

C. G., a thirty-two year old Negro, was admitted to Cook County Hospital, May 3, 1950, with the diagnosis of "acute urinary retention." Two days prior to admission the patient noted the onset of "crampy" pains in the lower abdomen, which gradually increased in severity. The pains were intermittent, similar to "gas pains" and relieved by the passage of flatus. The bowels were normal and

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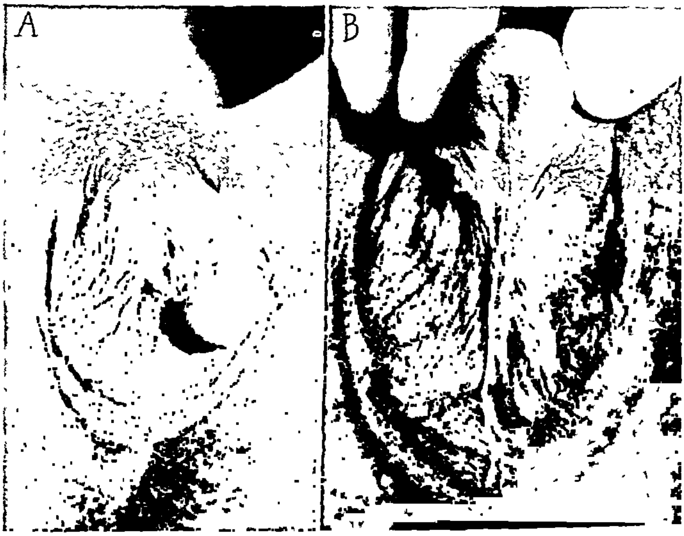

FIG. 1. *A*, external genitalia. *B*, urethral opening in lower end of perineal furrow

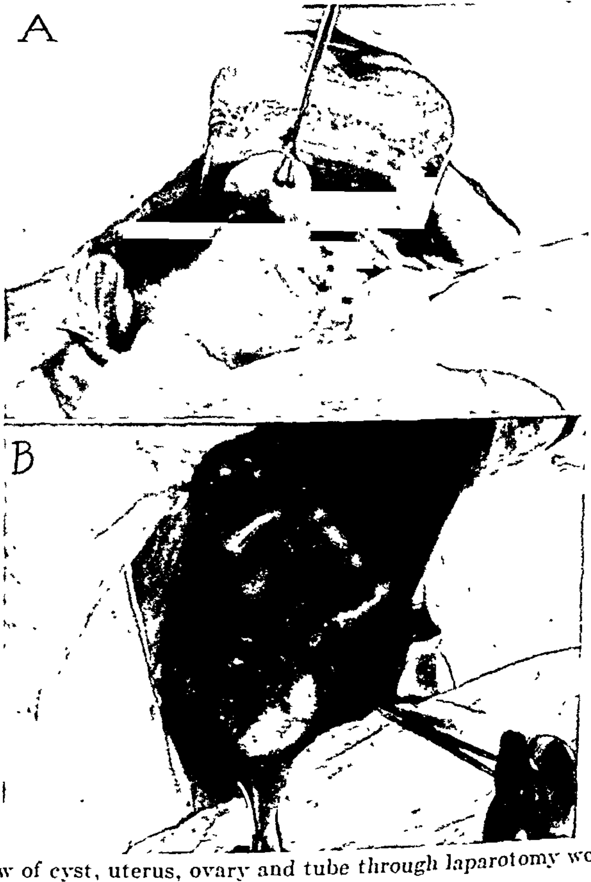

FIG. 2. *A*, view of cyst, uterus, ovary and tube through laparotomy wound. *B*, view of testis after removal of cyst, uterus and ovary.

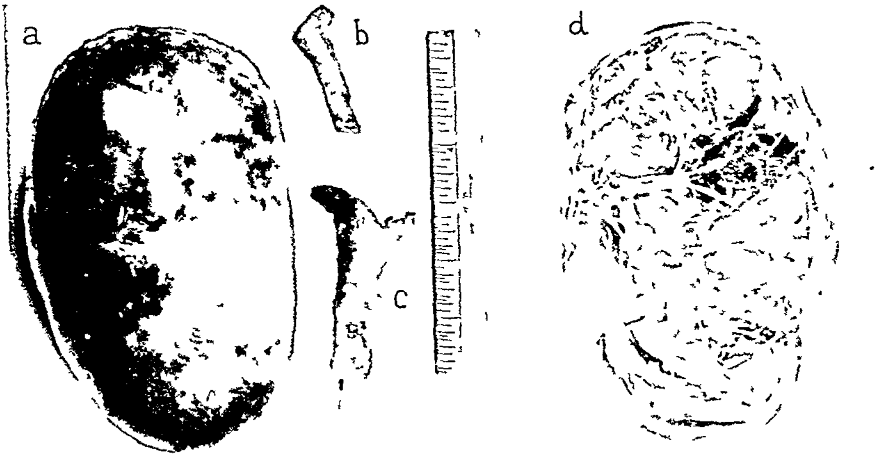

FIG 3 A, gross specimens Left, cystic mass, right upper, fallopian tube, right lower, infantile uterus and cervix B, cross section of cystic mass

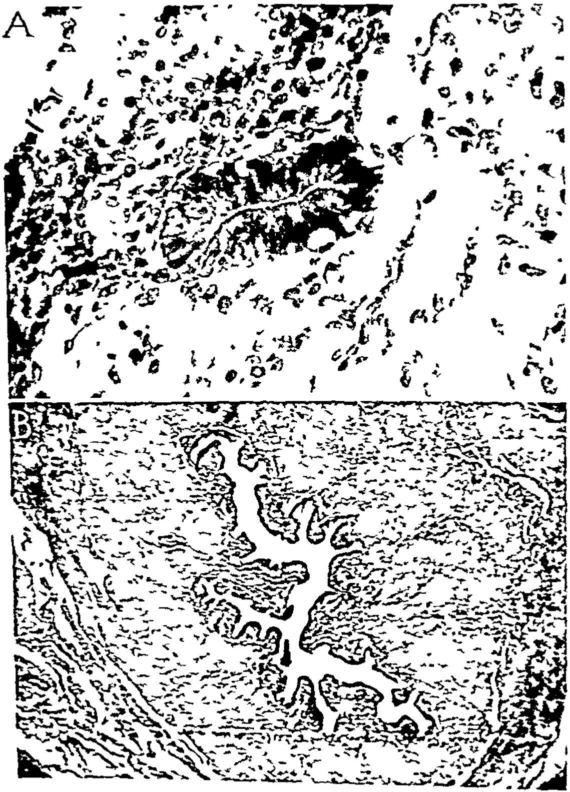

FIG. 4 A, endometrial gland and stroma, section from body of uterus B, fallopian tube structure in wall of uterus

there were no genito-urinary complaints. Anorexia, nausea and vomiting were present the day of admission. A system review was negative except for frequent colds with periodic hemoptysis which might have been considered as vicarious bleeding. He was a janitor in a local theatre. He had been married 3 years and his wife had never been pregnant. Intercourse was stated to be normal and semen was ejaculated. The patient weighed 118 pounds and was 4 feet, 11 inches tall. His temperature was 98.6F, pulse was 104, and respirations were 22. Blood pressure was 116 systolic and 80 diastolic. The hair distribution appeared normal. Abdominal examination revealed a round smooth mass, the size of a grapefruit, which was palpable just above the symphysis. There was dullness on percussion. This was first thought to be a full bladder. Urethral catheterization did not alter the size of the mass. Inspection of the genitalia revealed a small hypoplastic penis with a hypospadiac opening at the penoscrotal junction (fig. 1). No testes were palpable in the scrotum. A rectal examination revealed a small flat prostatovesicular bed.

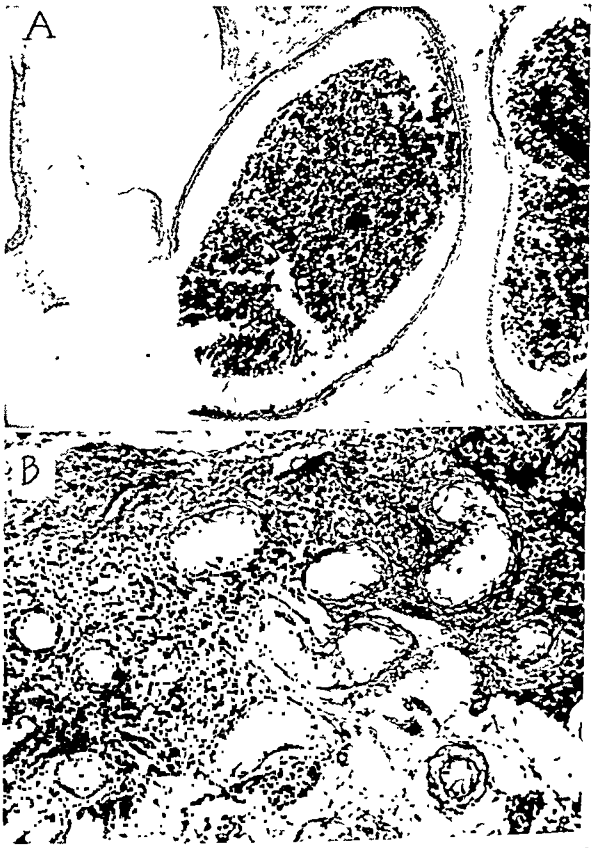

FIG. 5. *A*, section from epididymis. B, atrophic testicular tissue and Leydig cells

A routine roentgen ray study demonstrated a suprapubic mass of soft tissue density in the region of the bladder. X-ray of the chest was negative. Abdominal cramps remained the chief complaint during the time of study. Cystograms confirmed the extrinsic mass.

Cystoscopic examination revealed no evidence of a prostate but there was a small ridge in the posterior urethra, which showed gaping prostatic ducts. The trigone appeared normal but there was encroachment upon the posterior wall of the bladder from extravesical pressure. Retrograde urograms revealed a double ureter on the right side. The blood serology was negative and blood chemistry values were within normal limits. The urine was normal. Barium studies of the bowel revealed no lesions.

An exploratory laparotomy was performed on June 19, 1950, through a right paramedian incision. Upon entering the peritoneal cavity a large cystic mass the size of a grapefruit presented itself and appeared as an ovarian cyst or tumor. Further inspection revealed a right tube and ovary with an infantile uterus (fig. 2, *A*). The right tube and ovary overlaid a right abdominal testis (fig. 2, *B*). An ovary or a testis on the left side could not be found.

The cystic mass was removed and a total hysterectomy and right salpingo-oophorectomy performed. A biopsy was taken from the abdominal testis. Postoperative convalescence was uneventful. Surgical correction of the hypospadias was refused.

Pathological report (Dr. Alex B. Ragins): "The specimen consists of three pieces of tissue (fig. 3, *A*). The first measures 7.5 by 1 by 0.4 cm. and grossly appears to be a fallopian tube. On pressure the opaque, greyish white tissue within the lumen is freely movable and the surface is light brown to greyish in color.

"The second fragment of tissue measures 7.5 by 2.5 by 1.5 cm. and resembles a bicornuate uterus with an elongated cervical canal and a cervix (fig. 3, *A*). The cervical portion is greyish white in color. On section of the body of the uterus the lumen appears fenestrated. The cornual portion has a thick wall and contains a central smaller lumen."

"The third tissue is composed of a cystic mass measuring 18 by 12 by 7.5 cm. and is partially covered by adherent omental fat (fig. 3, *A*). The surface is thickened and greyish white in color. The wall measures up to 5 mm. in thickness and the lumen is filled with a liquid which is partly gelatinous fluid (fig. 3, *B*). The inner wall reveals a multilocular appearance, filled with a bloody gelatinous fluid. On stripping the multilocular layer from the cyst wall, one encounters a permanent, greyish white membrane which resembles skin."

"In one area on the free surface is a vestigial-like tubal structure resembling a fallopian tube, which is markedly adherent. However, no lumen is evident on section.

"Microscopic: Section of the portio cervix reveals a typical cervical mucosa, characterized by the presence of tall columnar epithelial cells. Section of the body of the structure reveals endometrial-like glands in a proliferative phase, with slight cystic dilatation of the ducts (fig. 4, *A*). Section of the cornual portion of the uterus reveals a lumen lined by tall columnar epithelium, representative of a fallopian tube lining (fig. 4, *B*). Section of the structure which grossly suggests epididymis reveals an acinar structure which is lined by cuboidal epithelium, and also a small structure at one pole, which is suggestive of a fallopian tube (fig. 5, *A*). Section of the cyst reveals a nondescript cyst wall composed of dense fibrous connective tissue and numerous blood vessels. Section of the mass from the right groin reveals atrophic testicular tissue, undescended, which is associated with marked proliferation of the interstitial cells of Leydig (fig. 5, *B*)."

This picture is compatible with the diagnosis of intersex.

SUMMARY

An instance of hermaphroditism in a 32 year old Negro is reported. He had all the normal reactions of any male. Laparotomy revealed a uterus, one fallopian tube and ovary and one testis. The removal of his uterus and ovaries did not change his former male reactions. No clinical studies were made of the estrogens or androgens in this patient.

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ADVANTAGES OF THE CHERNEY INCISION FOR UROLOGIC OPERATIONS

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Many of the lesions with which the urologist is confronted are so situated within the less accessible regions of the body that the problem of surgical approach and exposure remains an ever-present challenge. Despite innumerable advances in operative technique and more profound knowledge of regional anatomy and physiology, deep-seated lesions within the bony pelvis continue to be especially troublesome.

In the search for better avenues of exposure, certain fundamental truisms regarding surgical incisions must be considered. The incision should be so placed as to give the best possible access to that part of the operative field where the most difficulty is anticipated; it should not cause any serious disruption of nerve or vascular supply; it should be adequate in length and capable of being extended without damage; it should interfere as little as possible with respiratory function in the immediate postoperative period; and it should leave a strong durable scar.

Vertical lower abdominal incisions no doubt have earned a permanent place in urologic surgery, but they unquestionably have definite limitations, especially when one is working in the lateral recesses of a deep pelvis. Dissatisfaction with vertical incisions is manifested by the increasing popularity of transverse lower abdominal incisions for many types of operations. Even a casual review[1-3] of urologic literature promptly reveals that more and more operations are being performed through some type of transverse incision.

It is not our purpose to delve extensively into the anatomic and physiologic considerations of all the various types of incisions. These factors have been handled masterfully by several other authors.[4-7] Suffice it to say, transverse incisions not only provide better exposure of pelvic and lower abdominal structures, but they also fulfill the other foregoing criteria of an acceptable incision.

Read at annual meeting, North Central Section, American Urological Association, Toledo, Ohio, October 4, 1951, and at meeting of Oklahoma State Medical Association, Oklahoma City, Oklahoma, May 19, 1952.

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Baudelocque[8] used a transverse incision for cesarean section as early as the first part of the nineteenth century. In 1900 Pfannenstiel[9] described his well-known transverse incision for pelvic operations. Maylard[10] in 1907 and Boeckmann[11] in 1910 independently described transverse abdominal incisions which severed all layers of the anterior wall at the same level. Both the Pfannenstiel and the Maylard types of incisions are still in vogue, but each has had its opponents. Some surgeons have objected especially to any incision that sections all layers of the abdominal wall in the same plane.

In 1941 Cherney[12] described a transverse incision for low abdominal operations which he thought had overcome objections to both the Pfannenstiel and Maylard incisions and at the same time had combined the attractive features of both Excellent exposure of the lower part of the abdomen and entire pelvis was obtained without dividing the rectus muscles in the plane of the skin or fascial incisions. Smith[13] in 1946 first reported the application of Cherney's incision to urologic operations. More recently Wayman[14] mentioned its use in the surgical treatment of megalo-ureter. In all probability there have been other publications in which use of the Cherney incision has been mentioned for urologic procedures.

We have been impressed by several commendable features of the Cherney incision. Magnificent exposure has been obtained in obese as well as thin patients. Scars from previous suprapubic operations have not made this type of exposure more difficult. It not only has been ideal for procedures on the bladder and adjacent structures, but has afforded ample visibility for transplantation of the ureters and exploration of the peritoneal cavity. Furthermore, lateral extension of the conventional Cherney incision has permitted simultaneous operations on the upper part of the urinary tract, including complete nephroureterectomy. Our patients have been astonishingly comfortable during the immediate postoperative period and so far there have been no hernias or eviscerations after employment of the following type of exposure.

TECHNIQUE

A convex transverse incision of the skin is made with the central portion of the incision approximately 2 fingerbreadths above the superior margin of the symphysis pubis. Each end is curved upward to a point medial to the anterior superior spine of the ilium (fig. 1). This incision is carried down through the panniculus, the aponeuroses of the external and internal oblique and the anterior sheath of the rectus muscles (fig. 2). Only the aponeurotic portions of the oblique muscles are

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incised. Any muscular fibers which may extend unusually close to the midline are left for subsequent splitting.

The transverse incision in the anterior sheath exposes the recti and sometimes the upper limit of the pyramidalis muscles. While the inferior flap of the sheath is being retracted, each rectus muscle is separated from the lower portion of the anterior sheath by blunt dissection after a few septal strands of fibrous tissue have been cut (fig. 3). The pyramidalis muscles usually remain attached to the sheath but should they extend higher than the transverse incision, they may be left attached to the recti.

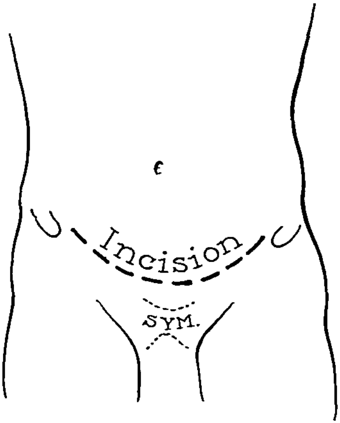

FIG. 1. Location of skin incision.

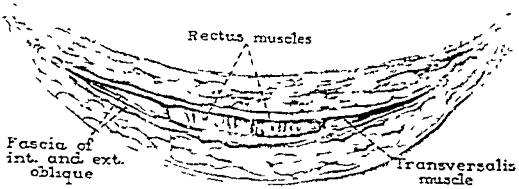

FIG. 2. Incision of anterior sheath of recti and aponeuroses of external and internal oblique muscles.

While the inferior flap is retracted, the lower ends of the recti are freed by inserting the index finger along the lateral margins just above the symphysis and separating the posterior surface of the recti by blunt dissection until the fingertips meet near the midline. With the finger of one hand supporting the muscles and holding away underlying structures, the tendinous insertions of the recti are divided with scissors close to the symphysis, along the line shown in figure 3.

The recti are elevated and separated from the underlying tissues by blunt dissection to a point well above the level of the original incision in the skin (fig. 4). The transversalis fascia and muscle fibers are split laterally on each side as the recti are being reflected. Any unusual extensions of the external oblique muscle fibers are dealt with in similar fashion. The inferior epigastric vessels are encountered lateral to the recti and are usually ligated and divided (fig. 4). No other major vessels are encountered.

An incision of this magnitude affords excellent exposure of the extraperitoneal pelvic structures and should be sufficient for all procedures on the bladder, prostate and lower end of each ureter. Transverse opening of the peritoneum, along the line suggested in figure 4, also permits thorough exploratory palpation of all intraperitoneal structures and adequate visualization of the lower abdominal contents. Simultaneous ureterosigmoidostomy and total cystectomy have been performed most satisfactorily with this type of exposure. When the patient is in Trendelenburg position and the intestines are held back with a moist abdominal pack, the effect may be likened to that which might be obtained if a half-moon segment of the lower abdominal wall were dissected away. There is

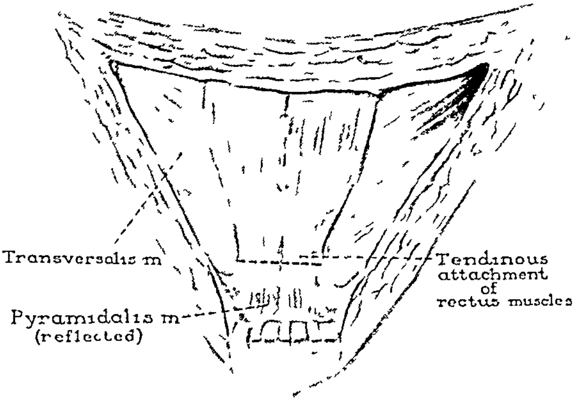

FIG 3 Exposure of tendinous insertion of recti on symphysis and proposed level for division of tendons.

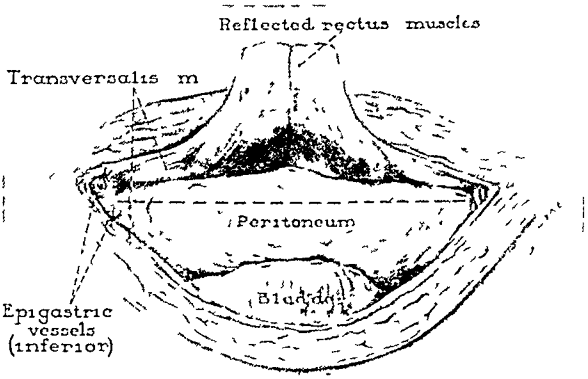

FIG. 4 Recti reflected upward after splitting transversalis muscle, exposing bladder, peritoneum and proposed location of peritoneal incision

an unobstructed view of the sigmoid colon, ureters from the level of the sacral promontory down, bladder and other pelvic organs. Gentle retraction around the periphery of the field will of course improve exposure in specific areas.

Closure of the incision is accomplished in layers. The peritoneum is closed with a continuous suture of no. 1 chromic catgut (fig. 5). The patient is then leveled and the ends of the tendons of the recti are re-approximated to the periosteum of the symphysis or to the under surface of the anterior sheath near the pubes with four or more interrupted mattress sutures of silver or steel wire (fig. 6). Cherney specifically advises reattachment to the sheath instead of to the symphysis. We have tried both sites, have found both quite satisfactory and now merely elect to use the one that may be more convenient. The recti usually reach the symphysis without tension, provided muscular relaxation has been maintained and the Trendelenburg position has been corrected completely. When drainage is necessary a Penrose drain is brought out at the lateral margin of each rectus muscle.

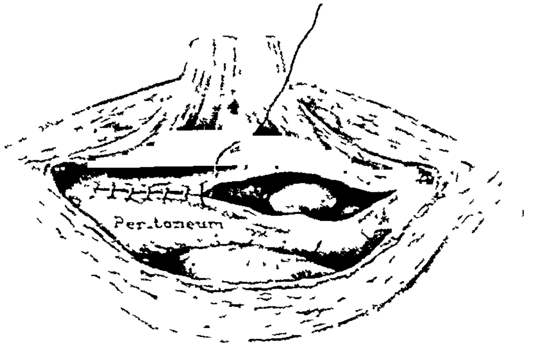

Fig. 5. Closure of peritoneum.

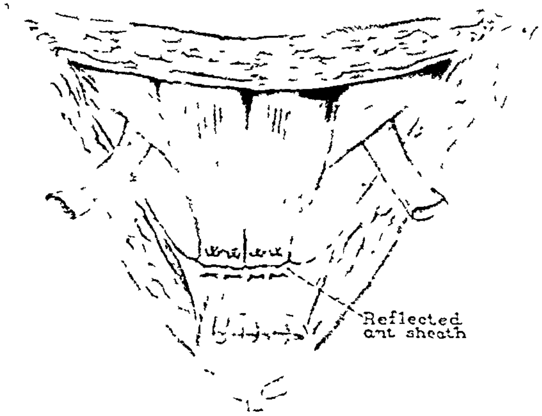

Fig. 6. Reattachment of rectus tendons.

Split fibers of the transversalis and oblique muscles are approximated with interrupted sutures of no. 1 chromic catgut after which similar sutures are used to close the aponeuroses. The latter may be sutured in two layers if desired. The same type of closure is used for the defect in the anterior sheath of the recti (fig. 7).

The superficial fascia and subcutaneous tissues are sutured with interrupted plain catgut and the skin is closed with black silk. Attention is directed to the fact that the sutures in the peritoneum, rectus tendons and fascias are in different planes with no overlapping.

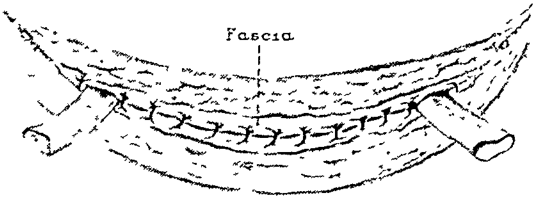

FIG. 7. Closure of anterior sheath of recti and aponeuroses of oblique muscles.

TABLE 1. *Operations through Cherney incision*

- *Urethra*
  - Plastic operation for epispadias
  - Prostatectomy
- *Bladder*
  - Total cystectomy
  - Segmental resection
  - Diverticulectomy
  - Cystolithotomy
  - Obliteration of vesical neck
  - Permanent cystostomy
- *Ureter*
  - Ureterosigmoidostomy
  - Cutaneous ureterostomy
  - Ureterectomy
  - Ureteroneocystostomy
- *Kidney*
  - Nephro-ureterectomy
- *Others*
  - Loop colostomy
  - Orchiectomy
  - Internal repair of inguinal hernia
  - Exploration and biopsy

APPLICATIONS

To date we have used some form of the Cherney incision in 56 cases. Most of these operations were multiple procedures. Whereas it initially was our practice to employ this incision only when simultaneous bilateral ureterosigmoidostomy and total cystectomy were contemplated, we have now come to use it by preference for a variety of urologic operations within the pelvis and lower part of the abdomen. Table 1 indicates the various types of procedures in the current series. Most of these were performed through the conventional incision shown in figure 8. It proved to be admirably suited for use in the stocky, obese patient with a thick panniculus and a large amount of intra-abdominal fat. However, we have used it to a comparable advantage in thin, asthenic patients as well.

The Cherney incision proved to be especially useful for other simultaneous, bilateral ureteral operations, such as bilateral cutaneous ureterostomy as illustrated in figure 8.

We were particularly impressed by the ease with which exposure could be improved by simply extending the appropriate limb of the incision toward the flank. In 2 instances extensions of 6 to 8 cm. (fig. 9) permitted ligation of the renal pedicle under vision and made it possible to perform complete nephroureterectomy as well as segmental resection of the bladder. A short extension of the left limb in another case made it simple to exteriorize an area of diverticulitis of the sigmoid as a loop colostomy after it had been separated from a perivesical abscess involving the dome of the bladder.

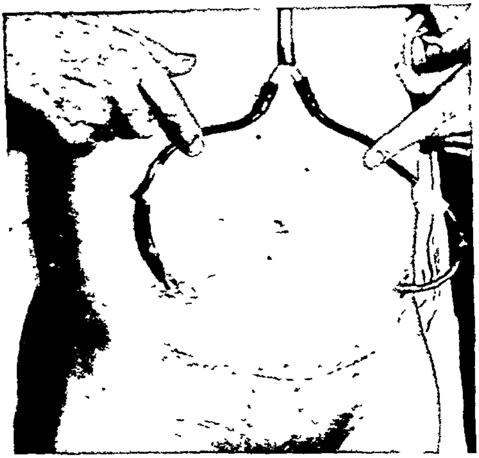

FIG. 8. Bilateral cutaneous ureterostomy performed through a Cherney incision.

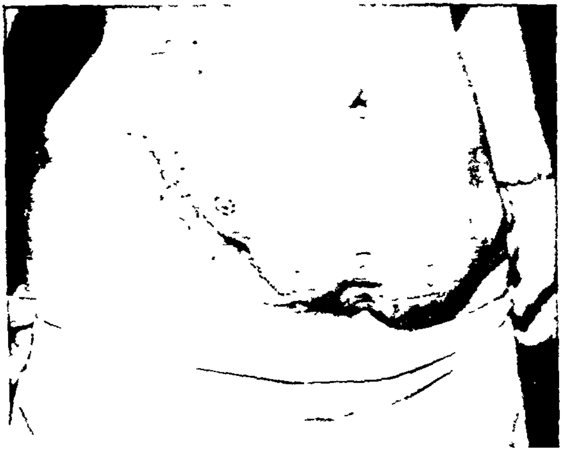

FIG. 9. Lateral extension of conventional Cherney incision for nephro-ureterectomy.

When it is a foregone conclusion that the contemplated operation will be confined to one side of the pelvis or abdomen or both, the incision can be placed mostly in that area, as demonstrated by figure 10. In this particular case most of the ureter had been left in situ after nephrectomy for a papillary tumor of the renal pelvis. A previous attempt elsewhere to remove the ureter through a midline incision had been unsuccessful. The long segment of tumor-bearing ureter and a cuff of bladder were excised easily through this modification of the Cherney incision despite the fact that the patient weighed 280 pounds.

Many of our patients had had previous suprapubic operations (figs. 9 and 10). Not only did these fail to complicate our Cherney incisions, but frequently the scar tissue seemed to make the final closure easier. Although the time necessary for closure of the Cherney incision may be longer than that required for repair of most vertical incisions, we are convinced that the improved exposure shortens the total operating time.

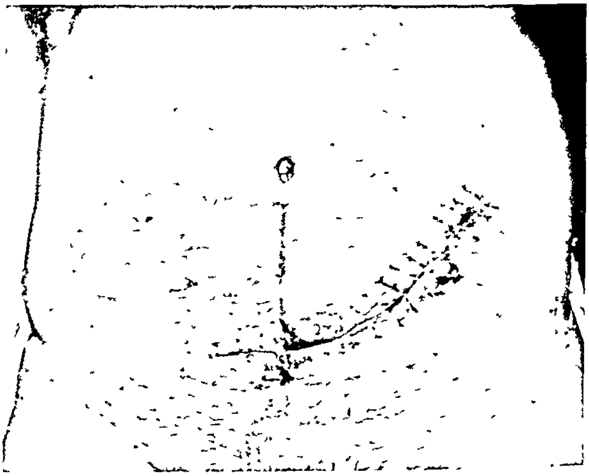

FIG. 10. Modified Cherney incision for removal of left ureter.

COMPLICATIONS

We have had no wound disruptions or eviscerations in any of our 56 cases. In some, profuse seropurulent or purulent drainage developed because of the infected nature of the original lesion. Even though the drainage was protracted in a few cases, lasting four weeks in 1 instance, all the incisions healed solidly.

There has been no osteitis pubis even though the recti were sutured to the symphysis in many cases.

To date we have had no incisional hernias, although admittedly the time interval since operation has not been long enough in all cases to exclude this possibility.

Very little has been published regarding the experiences of other surgeons with this type of incision. In their paper on ureterosigmoidostomy, Cordonnier and Lage[15] mention 4 postoperative eviscerations and 3 incisional hernias which they attributed to "the modified Cherney incision." In a recent personal communication Cordonnier[16] states that he still uses the Cherney incision for the repair of vesicovaginal fistulas and thinks it "gives an exposure far superior to that ob-

[15] Cordonnier, J. J. and Lage, W. S. An evaluation of ureterosigmoid anastomosis by mucosa-to-mucosa method after two and one-half years' experience. Tr South Central Sect., Am. Urol. Assn , p. 89, 1950.

[16] Cordonnier, J. J.· Personal communication to the authors.

tained by midline incisions," but has abandoned it for cystectomy and ureteral transplantation, after trying it in approximately 25 cases. It may be significant that the recti were reattached to the symphysis in all his cases for he mentions that "in many instances considerable difficulty was encountered in obtaining a firm attachment because the sutures at the symphysis would frequently pull out."

Carroll[17] has used the Cherney incision on approximately 25 patients for either cystectomy or radical retropubic prostatectomy and seminal vesiculectomy and has been enthusiastic about the exposure. One of his patients developed a hernia on the right side after cystectomy but this was repaired easily and the patient is well three and a half years later.

Fallis[18], who first persuaded us to try this type of exposure, and his associates have used the Cherney incision for approximately 100 anterior resections of the bowel with 1 hernia. This occurred in a woman whose enlarged uterus had to be brought so far forward in order to complete the intestinal operation that the recti would no longer reach the symphysis or inferior portion of the sheath and were left unattached. Fallis readily admits that hysterectomy would have been a valuable adjunct under these circumstances. In all his other cases the recti were sutured to the symphysis, despite which there were no hernias, osteitis or eviscerations.

Cherney[19] has informed us that he has personal knowledge of the use of his incision in approximately 500 cases, more than 100 of which were his own, with development of an incisional hernia in only 1 case. There have been no disruptions of the wound to his knowledge

In all probability any type of abdominal incision may permit the development of hernia or evisceration under certain circumstances but there does not seem to be any conclusive proof that the Cherney incision is more vulnerable than vertical or other varieties of transverse incision. On the contrary, its record to date would appear to be exceptionally good in this respect and should not deter anyone from using it.

SUMMARY

In making a plea for more extensive utilization of a low abdominal transverse incision for urologic operations, we have reviewed the application and technique of the Cherney incision as we have successfully employed it for a variety of urologic procedures. Improved exposure is frequently the "key" which transforms a difficult operation into a relatively easy one. We are convinced that the Cherney incision has many inherent advantages that cannot be equalled by other types of incisions and that the difficult pelvic operations which so frequently confront the urologist can be performed with less "wear and tear" on both the patient and the surgeon if the Cherney incision is used.

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[17] Carroll, Grayson: Personal communication to the authors.
[18] Fallis, L. W.: Personal communication to the authors.
[19] Cherney, L. S.: Personal communication to the authors.

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A SIMPLIFIED METHOD FOR ESTIMATING URINARY INORGANIC PHOSPHATE DURING ALUMINUM GEL THERAPY FOR PHOSPHATIC CALCULI*

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The purpose of this note is to describe a simplified method for estimating the 24 hour urinary level of inorganic phosphorus. This procedure has been designed to assist in the optimal use of the aluminum gel regimen developed in this laboratory for the prevention of recurrences or further growth of renal phosphatic calculi.[1]

The objective of this regimen is to reduce urinary phosphorus excretion to levels at which the precipitation of this ion with calcium, ammonium or magnesium could take place with difficulty or not at all. This is accomplished by aluminum gels through the formation of insoluble aluminum phosphate salts in the intestinal tract, with a corresponding reduction in the amount of phosphorus available for absorption. This diversion of phosphorus excretion via the intestinal tract leads to the prevalence of lower serum inorganic phosphorus values and thereby to a proportional diminution in the amount excreted in the urine. With a fixed dietary phosphorus intake at any given level, the aluminum gel dosage can be adjusted to achieve any desired urinary phosphorus excretion, 300 mg. or less of phosphorus/24 hours being regarded as optimal.

It is only possible to determine how faithfully this regimen is being adhered to by frequent determinations of the 24-hour urinary phosphorus excretion. Current methods for this analysis are sufficiently exacting as to require laboratory facilities beyond those usually available to the physician in his office; and this circumstance, as well as the cost of frequent analyses in commercial or hospital laboratories, has in the past been a formidable obstacle to the optimal application of this therapeutic regimen.

The analytical procedure to be described is based on the suggestion of Sumner[2] that the phosphomolybdic acid formed during the first step in the analysis of inorganic phosphorus be reduced by ferrous sulfate instead of by the conventional amino-naphthol sulfonic acid reagent.[3] A blue color is obtained which obeys Beer's law and remains stable for a number of hours. This color can be measured semi-quantitatively by means of a color comparator† equipped with permanent glass standards corresponding to known concentrations of phosphorus in a 24 hour urine specimen.

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* Aided by a grant from Wyeth, Inc., Philadelphia, Pa.
Accepted for publication May 1, 1952.

[1] Shorr, E. and Carter, A. C.: Aluminum gels in the management of renal phosphatic calculi. J.A.M.A., **144:** 1549, 1950.

[2] Sumner, J. B.: A method for the colorimetric determination of phosphorus. Science, **100:** 413, 1944.

[3] Fiske, C. H. and Subbarow, Y.: The colorimetric determination of phosphorus. J. Biol. Chem., **66:** 375, 1925.

† This comparator and kit No. 811 can be obtained from the Hellige Inc., 877 Stewart Ave., Garden City, N. Y.

The two permanent glass standards correspond to 200 and 300 mg. inorganic phosphorus per 24 hours. They are mounted in the comparator on either side of a slot for the test tube containing the unknown sample.

Two reagents are required for this test:

1) A 2.5 per cent ammonium molybdate solution (25 gm. $(NH_4)_6Mo_7O_{24} \cdot 4H_2O$ are dissolved and diluted to 1 liter with 5N H_2SO_4).

2) Ferrous sulfate crystals ($FeSO_4 \cdot 7H_2O$).

The test is carried out as follows:

1) The complete 24 hour urine sample is diluted to 3 liters with water and well shaken (at least 5 times) *just* before removing an aliquot for analysis.

2) Five cubic centimeters of the specimen are pipetted into a 100 cc volumetric flask and diluted to about 60 cc with water. Then 10 cc of the molybdate reagent are added and the mixture shaken.

3) Two grams of ferrous sulfate are now added, the flask is filled with water to the 100 cc mark and mixed until the crystals are completely dissolved, usually a matter of 5 minutes.

4) The blue color developed is now ready for comparison in the comparator. An aliquot is poured into the tube supplied with the comparator.

If no comparator is available, a stock phosphorus solution can be used to provide the standards for comparison. For quantitative analysis the color may be measured in a photoelectric colorimeter utilizing the two standard solutions for the calculation, the color formed obeying Beer's Law.

The stock phosphorus solution: 0.146 gm. KH_2PO_4 are dissolved and diluted to 1 liter with 0.1 N H_2SO_4. One cubic centimeter contains 33.33 micrograms phosphorus.

Ten and 15 cc of this stock solution corresponding respectively to 200 and 300 mg. inorganic phosphorus per 3 liters are added to 100 cc volumetric flasks and the procedure followed as described above for the unknown urine sample. The color comparison can be made directly from the volumetric flasks which should be of uniform shape.

With both comparator and standard solutions, there is no difficulty in estimating whether or not the 24 hour phosphorus output is above or below the desired 200 or 300 mg. Where the clinical status would seem to warrant even lower concentrations, the 200 mg. standard is particularly serviceable. The simplicity of the procedure lends itself readily to office use and indeed may be used at home by the patient, after instruction.

The superior stability of the color produced with ferrous sulfate as the reducing agent over the conventional amino-naphthol sulfonic acid reagent has led us to apply the above procedure to the quantitative analysis of inorganic phosphate in serum, urine and stool ashes.* The details of this method will be described elsewhere.[4]

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* While in the process of developing this procedure a method was published by Rockstein and Herron[4] incorporating Sumner's suggestion to use ferrous sulfate in the micro determination of inorganic phosphate.

[4] Rockstein, M. and Herron, P. W.: Colorimetric determination of inorganic phosphate in microgram quantities. Anal. Chem., 23: 1500, 1951.

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A NEW RESECTOSCOPE

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The modern instruments used today in prostatic resections are a far cry from the one used by Ambrose Paré in the sixteenth century. The era of practical cold cutting instruments began with the cold punch of Young[1] in 1909 and is continuing. The fact that perfection has not been reached is evidenced by the continued improvements that have been made on this basic design: Braasch in 1918,[2] Young in 1919,[1] Rose in 1925,[3] Bumpus in 1926,[4] Ravich in 1927,[5] Day in 1929,[6] Thompson in 1935.[7] In 1931, Kirwin[8] made a type of punch which cut a little differently. The practical instruments have been those modified by Braasch, Bumpus and Thompson, each improving the previous model in the order given.

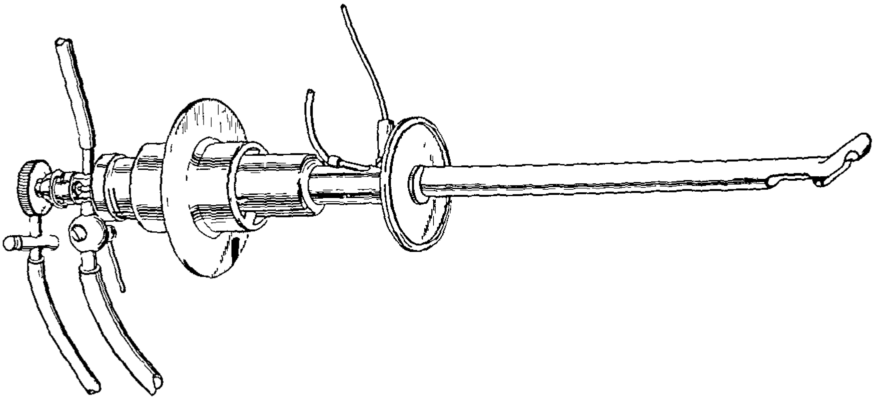

Fig. 1

Those who use the punch instruments are familiar with their limitations. Since his introduction to this type of instrument the author has believed that the cold punch could be improved to cut more efficiently and accurately. Consequently, the instrument herewith presented was produced after many changes in design and some production difficulty. It is designed to cut the tissue rather than to shear it out by a punch action. A shearing action or a punching action is a much less efficient method of soft tissue cleavage in comparison with a cutting action. The surgeon uses the knife to cut, not to chop with as an ax.

Accepted for publication April 14, 1952.

[1] Young, H. H. and Davis, D. M.: Young's Practice of Urology. Philadelphia and London: W. B. Saunders Co., 1926, vol. 2, p. 497.

[2] Braasch, W. F.: Median bar excisor. J.A.M.A., **70**: 758, 1918.

[3] Rose, D. K. A visual prostatic punch. Surg., Gynec. & Obst., **41**: 109, 1925.

[4] Modern Urology, edited by Hugh Cabot. Philadelphia: Lea & Febiger, 1936, vol. 1, p. 815.

[5] History of Urology. Baltimore: Williams & Wilkins, 1933, vol. 2, p. 170.

[6] *Ibid.* p. 171.

[7] Emmett, J. L.: Transurethral resection with the cold punch: Operative technique. J. Urol., **49**: 815, 1943.

[8] Kirwin, T. J.: Vesicle neck obstruction: Presentation of a new instrument for its relief. Surg., Gynec. & Obst., **52**: 1007, 1931.

In this new resectoscope (fig. 1) there is a rotary-reciprocal motion of the knife which cuts the tissue as the knife advances. Some of the advantages are: increased efficiency through an opening spring; a driving ring which enables the instrument to be rotated to any position while remaining in a comfortable position in the hands or hand; improved water inlet; increased cutting efficiency gained by knife rotation which does not push the tissue out of the fenestra as the punch does, thereby giving more accurate control of depth of cut and tissue removed with each stroke; friction lessened by ball bearings. All of these factors lead to a speedier resection, less operative time and blood loss and a smoother prostatic fossa.

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THE ELECTRO-UROGRAM

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It has been known for almost a hundred years that organic tissue is able to produce and transmit electrical currents. This property was first attributed to the muscle, and especially to the heart, but later it was shown that every tissue can emit electricity. Even for the kidney it was known that this organ can under certain circumstances create currents; pharmacological investigations referring to this phenomenon were published abroad about 15 years ago, but had no interest for, or influence on, urology.* Similar publications referred to the uterus and to the brain, and the use of the electrocardiogram and the encephalogram has produced definite achievements for human physiology, pathology, and clinical investigations.

This paper shall demonstrate the experimental and clinical work which has been done during the last 2 years to produce and to record electrical currents from the urinary tract. To get curves which, in consequence, will pave the way for a new method in renal diagnosis, one has to work with the urinary tract as a whole. The recording of electrical potentials from the kidney alone should be done only in experimental work; it does not suffice in man. The bladder, and therefore, the whole urinary system has to be taken into consideration when working on the Electro-urogram (EUG).

The EUG resembles in several ways, as in some technical steps, the electrocardiogram. Nevertheless, there are great differences between both, based on the different physiological conditions of the two organs. Thus, the heart muscle works continuously; the kidneys do not. In order to get the produced current for registration, we must put the kidneys to work by giving the animal or the human being enough fluid to initiate at least a fair diuresis. It seems that the curves originated by the left and right kidney are identical in their nature. Practically speaking, however, since the diuresis in one kidney never equals the output in the sister organ, the curves look different. Various amounts of fluid taken in produce various curves, as it can be easily demonstrated by experiment. The optimal amount of hypodermically injected saline while doing experiments on rabbits, was 50 cc.

The work was done with a General Electrocardiograph, model B, type 5.

The leads were set during the experiments on rabbits as follows:

1) The kidney was first exposed surgically in the usual way; it must be mentioned that the kidneys of the rabbit have, within the retroperitoneal space, a somewhat different position from the human kidney. Both electrodes were placed upon the surface of the kidney, so that the organ lay between them.

2) One electrode was put on the exposed kidney, the other one over the full bladder.

The author got every possible assistance from the Montana State Hospital, for which he wishes to express his sincere thanks.

* See Dungern, Biologia Generalis, vol. 12, p. 478.

Accepted for publication May 12, 1952.

3) A specially constructed electrode with a small, sharp needle (No. 25) was introduced into the kidney pelvis, the other electrode again placed on the bladder.

4) One electrode was inserted into the kidney pelvis, and the other one put in the region of the m. quadratus lumborum. Simultaneously, electrocardiograms were taken to demonstrate that the kidney curves contrast entirely from the electrocardiogram.

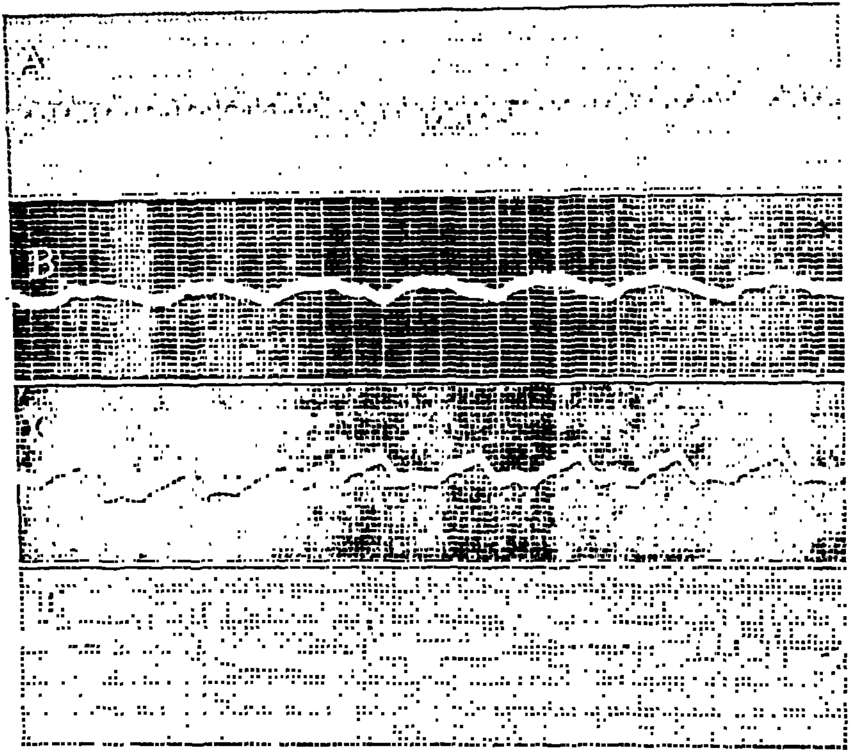

FIG. 1. *A*, electrocardiogram for comparison. *B*, EUG. Typical curve. *C*, EUG. Typical curve. *D*, EUG. Curve after severe traumatization of kidney.

The following system has been found most suitable after a long period of error concerning the cables which lead from the electrodes to the instrument. The right arm cable was taken for the right kidney, the left arm cable for the left kidney, and the left leg cable for the bladder. When the needle was introduced into the kidney pelvis, a precordial electrode was used. It was, according to the principles of the electrocardiogram, connected to the left leg cable, and the other electrode was attached to the left arm or right arm cable, respectively.

The moment that the kidney was traumatized, the damage extended from slight squeezing to the destruction of the organ. *The curves began to change immediately.*

So far, the whole investigation had some physiological and urological interest. When it has been found out that the curves change under pathological conditions, the work seemed to become most promising for human pathology and clinical urology.

Curves can be registered in human beings in a similar way and under the condition that strong diuresis takes place. The minimum amount to induce a sufficient kidney function which can be registered by the EUG is two to three cups of fluid, but it is better to take in one pint. It is advisable to let at least ten minutes elapse between the intake of the beverage and the start of the EUG. Water is preferable to fruit juice. It is necessary to take first a plain anteroposterior film to ascertain the position of the kidney.

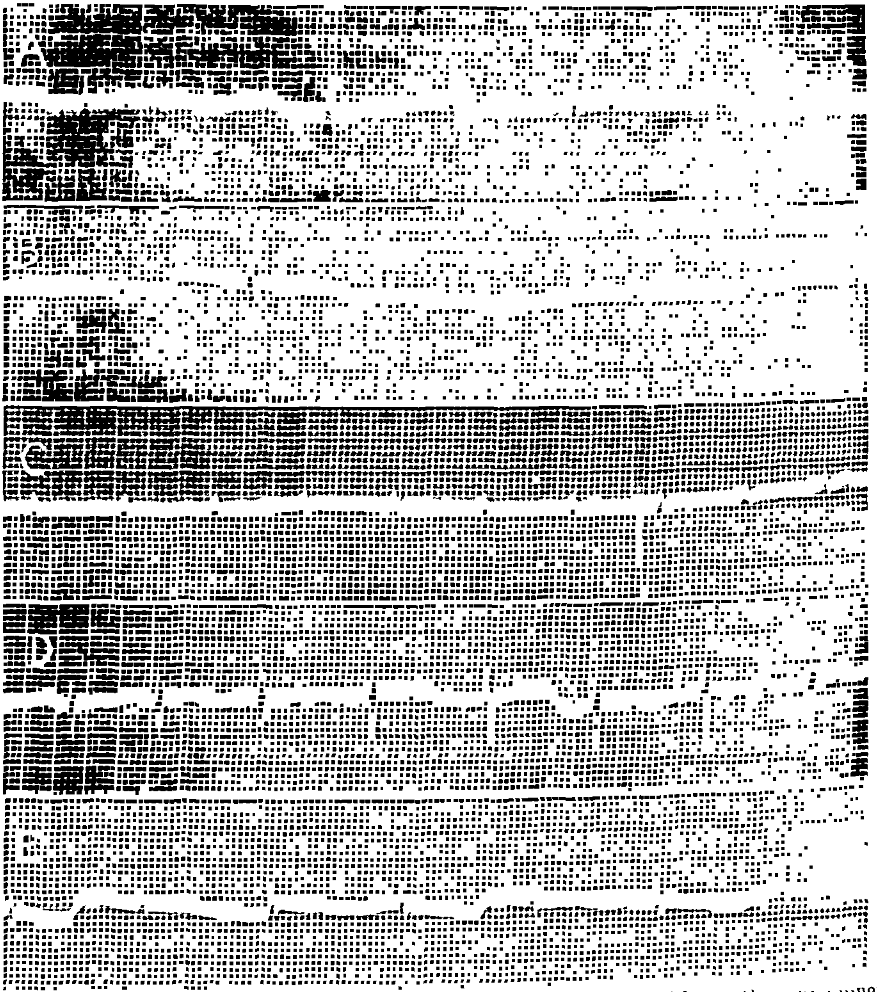

FIG 2 *A*, typical EUG Left kidney *B*, typical EUG Right kidney *C*, right kidney. Pyuria, hematuria and stone impacted in right ureter *D*, right kidney Four small concrements in renal pelvis *E*, same patient as *D* Different lead.

So far the following leads have been used in human beings:

1) One electrode on the costovertebral angle, as close as possible to the kidney; the cable used is the right or left arm cable, respectively. The second electrode is put upon the bladder region (left leg cable). It is advisable to work on a full bladder.

2) One electrode is set on the kidney, as described in the foregoing paragraph,

the other one within the bladder. The simplest way to do it is to place the silver wire, the so-called mandrin, within a ureteral catheter and to connect it with the precordial electrode. To introduce a ureteral catheter into a female bladder is, as everybody knows, very easy. In the male it is advisable to insert the ureteral catheter into a rubber catheter, Nelaton 18F for instance, to guide the latter into the bladder, and then push the ureteral catheter a little bit outside the rubber catheter through its eye, into the bladder. The EUG does not work if the ureteral catheter gets introduced through the metal shaft of a cystoscope.

3) The third lead is with one electrode placed in the region of the kidney. The second electrode is represented by the silver wire of a ureteral catheter inserted into the kidney pelvis of the kidney on the same side. On the outer electrode we use the right or left arm cable, respectively, and for the kidney pelvis electrode the left leg cable, since the ureteral catheter is connected with the precordial electrode.

4) The fourth lead is with one electrode placed on the full bladder. The second electrode is represented by the silver wire of a ureteral catheter inserted into the kidney pelvis, as described in paragraph 3. On the bladder we use the right or left arm cable, depending on which kidney is being examined; the silver wire, connected with the precordial electrode, is united with the left leg cable, as usual.

It is quite possible that during further development of the EUG new leads will be necessary.

We again witness the phenomenon that we have found in the kidney of the rabbit. The diseased or traumatized kidney gives curves different from those of the normal organ. Even a certain pressure exerted from outside by the fingers of the examining hand produce, in lean patients with weak muscles, curves different from the usual. The sensitivity of the electric current is great and, therefore, the EUG seems to be helpful in situations where the pyelogram fails. Every urologist is fully aware of the difficulties encountered in the early diagnosis of pathological conditions in the kidney. Usually the interior of the bladder is entirely visible; and in the few cases where inspection is impossible, the cystogram does the job. This is not true for the kidney, since this organ cannot be visually inspected. How often the early diagnosis of a hypernephroma is impossible, because the pyelogram is not meticulous enough to permit the correct diagnosis. If we cannot confirm our suspicion by palpation, the examination of the excreted urine, and the various methods of x-ray, the whole procedure is questionable. Although it is too early to draw definite conclusions, there are indications that the EUG will fill this gap and, after more work has been done and experience gained with it, it will successfully compete with all other means in the diagnosis of kidney diseases.

Urologists, although not used to reading curves, as psychiatrists and cardiologists are, will have no trouble in interpreting these curves, which is usually no more difficult than to learn how to read pyelograms.

Finally, another point should not be overlooked. The pyelogram is expensive, whereas the single EUG costs about 15 cents, a fact which is not negligible from the standpoint of economy.

Here attached are a number of typical curves of rabbits as well as human beings (figs. 1 and 2).

Curves can be registered in human beings in a similar way and under the condition that strong diuresis takes place. The minimum amount to induce a sufficient kidney function which can be registered by the EUG is two to three cups of fluid, but it is better to take in one pint. It is advisable to let at least ten minutes elapse between the intake of the beverage and the start of the EUG. Water is preferable to fruit juice. It is necessary to take first a plain anteroposterior film to ascertain the position of the kidney.

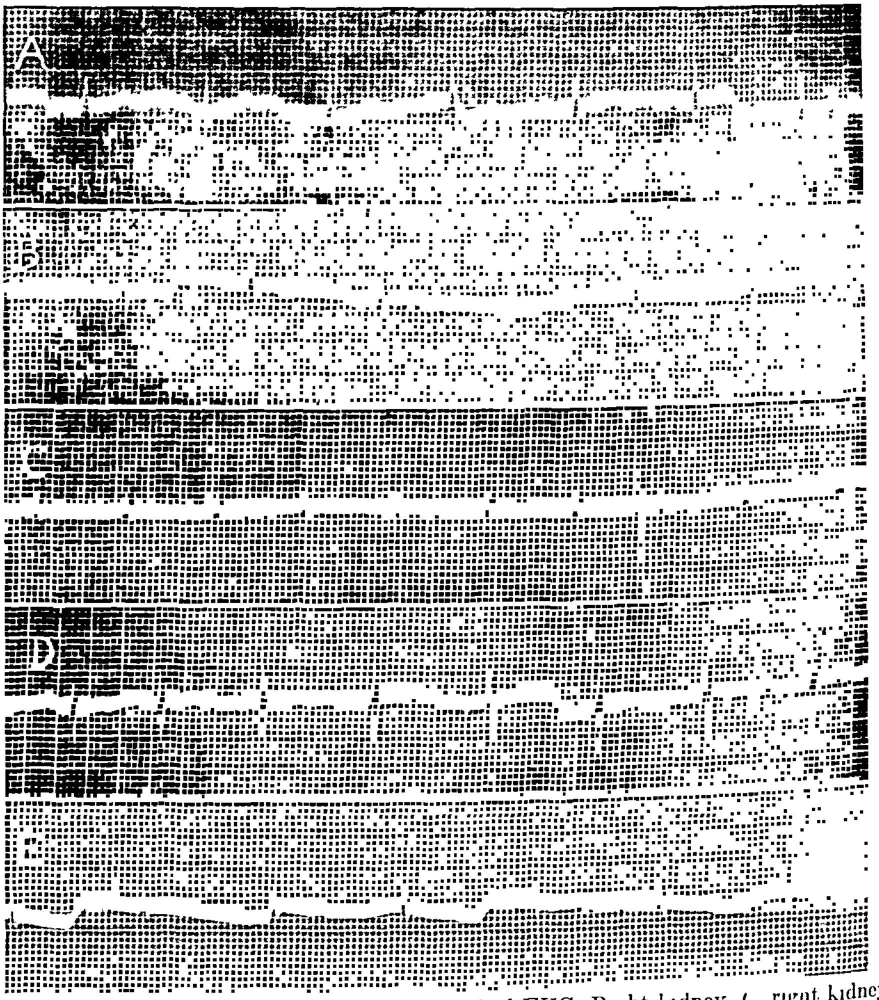

FIG 2 *A*, typical EUG. Left kidney *B*, typical EUG Right kidney. *C*, right kidney. Pyuria, hematuria and stone impacted in right ureter. *D*, right kidney Four small concrements in renal pelvis *E*, same patient as *D* Different lead.

So far the following leads have been used in human beings:

1) One electrode on the costovertebral angle, as close as possible to the kidney; the cable used is the right or left arm cable, respectively. The second electrode is put upon the bladder region (left leg cable). It is advisable to work on a full bladder.

2) One electrode is set on the kidney, as described in the foregoing paragraph,

the other one within the bladder. The simplest way to do it is to place the silver wire, the so-called mandrin, within a ureteral catheter and to connect it with the precordial electrode. To introduce a ureteral catheter into a female bladder is, as everybody knows, very easy. In the male it is advisable to insert the ureteral catheter into a rubber catheter, Nelaton 18F for instance, to guide the latter into the bladder, and then push the ureteral catheter a little bit outside the rubber catheter through its eye, into the bladder. The EUG does not work if the ureteral catheter gets introduced through the metal shaft of a cystoscope.

3) The third lead is with one electrode placed in the region of the kidney. The second electrode is represented by the silver wire of a ureteral catheter inserted into the kidney pelvis of the kidney on the same side. On the outer electrode we use the right or left arm cable, respectively, and for the kidney pelvis electrode the left leg cable, since the ureteral catheter is connected with the precordial electrode.

4) The fourth lead is with one electrode placed on the full bladder. The second electrode is represented by the silver wire of a ureteral catheter inserted into the kidney pelvis, as described in paragraph 3. On the bladder we use the right or left arm cable, depending on which kidney is being examined; the silver wire, connected with the precordial electrode, is united with the left leg cable, as usual.

It is quite possible that during further development of the EUG new leads will be necessary.

We again witness the phenomenon that we have found in the kidney of the rabbit. The diseased or traumatized kidney gives curves different from those of the normal organ. Even a certain pressure exerted from outside by the fingers of the examining hand produce, in lean patients with weak muscles, curves different from the usual. The sensitivity of the electric current is great and, therefore, the EUG seems to be helpful in situations where the pyelogram fails. Every urologist is fully aware of the difficulties encountered in the early diagnosis of pathological conditions in the kidney. Usually the interior of the bladder is entirely visible; and in the few cases where inspection is impossible, the cystogram does the job. This is not true for the kidney, since this organ cannot be visually inspected. How often the early diagnosis of a hypernephroma is impossible, because the pyelogram is not meticulous enough to permit the correct diagnosis. If we cannot confirm our suspicion by palpation, the examination of the excreted urine, and the various methods of x-ray, the whole procedure is questionable. Although it is too early to draw definite conclusions, there are indications that the EUG will fill this gap and, after more work has been done and experience gained with it, it will successfully compete with all other means in the diagnosis of kidney diseases.

Urologists, although not used to reading curves, as psychiatrists and cardiologists are, will have no trouble in interpreting these curves, which is usually no more difficult than to learn how to read pyelograms.

Finally, another point should not be overlooked. The pyelogram is expensive, whereas the single EUG costs about 15 cents, a fact which is not negligible from the standpoint of economy.

Here attached are a number of typical curves of rabbits as well as human beings (figs. 1 and 2).

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A CONDOM-COUPLED URINAL FOR INCONTINENCE

DAVID P. PAULL

From the Paraplegia Service, Cushing Veterans Administration Hospital, Framingham, Mass.

The commercially available urinal coupling attachments for the incontinent male patient leave much to be desired in cleanliness, lightness and convenience. Excoriation and ulceration of the skin of the penis may occur. The attachments which rely on circumferential pressure on the penis may also cause urethral dilatation, urethral diverticulum and peri-urethral abscess. Penile clamps may have the same effects. The apparatus here described, if properly used, will not cause any of these complications. It has been tried extensively on paraplegic patients with stress incontinence, with generally satisfactory results, and should be no less useful to other incontinent patients.

The coupling apparatus consists of a piece of latex rubber tubing, a plastic adaptor and a condom.

The tubing has an inside diameter of $\frac{3}{16}$ of an inch and an outside diameter of $\frac{3}{8}$ of an inch. The thickness of the wall prevents kinking. The small lumen allows the surface tension of the urine to maintain a column of fluid in the tubing, which exerts a constant negative pressure and so keeps the condom empty. Drainage is into an ordinary rubber leg urinal to which the distal end of the tubing is connected.

The adaptor, which is fully described in the drawings, is made of clear (Lucite) plastic. The tubing is passed into the condom, the end of which is then forced into the lumen of the tube by the narrow end of the plastic adaptor; the condom is then punctured through the lumen of the adaptor and reversed. (See figures 1, 2, 3.)

A ring of facing cement (latex, zinc oxide and benzene) is applied to the shaft of the penis distal to the penoscrotal junction, and the condom is rolled over the penis and pressed firmly over the cement-bearing area. It is light and flexible enough to obviate pressure or constriction.

When used in patients with neurogenic vesical dysfunction, as in the paraplegics for whom it was first devised, this apparatus must be considered as a supplement to rather than a substitute for appropriate bladder training, and for such patients its constant use is not advised. In other incontinent patients, where it may be worn for considerable periods of time, the condom should be replaced after about eight hours. The cement should be gently rubbed off the skin, not removed by solvents, and the penis washed and dried. The longer the interval before reapplying the apparatus, the better. The adaptor is cleaned with soap

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Accepted for publication February 4, 1952.

Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion of the Veterans Administration.

The author is indebted to Mr. Joseph Cabo of the Manual Arts Therapy Department of Cushing Veterans Administration for his assistance in the manufacture of the adaptor and the preparation of the drawings.

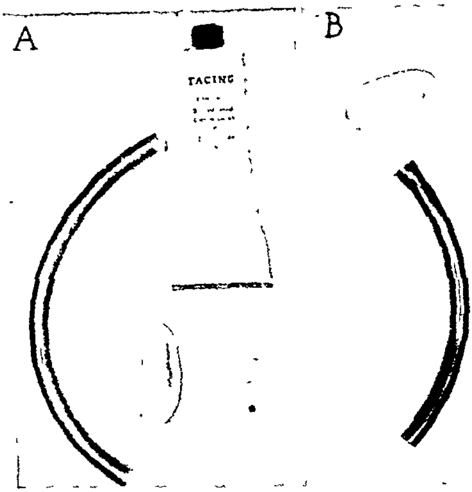

FIG. 1. *A*, component parts of coupling attachment, adaptor being shown in end and side views. *B*, assembled coupling.

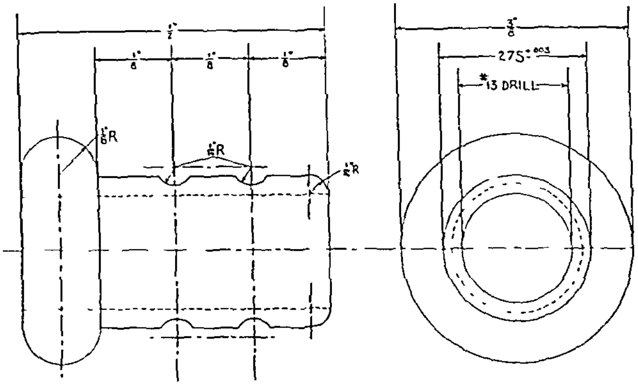

FIG. 2. Working drawings of plastic adaptor

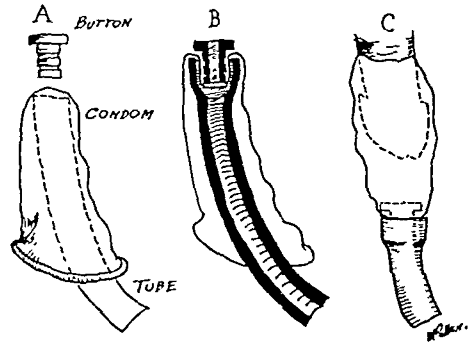

FIG. 3. *A*, inverted condom with adaptor about to be inserted. *B*, condom forced into tubing by adaptor. *C*, condom has been punctured, reversed and applied to penis.

and water. It may be sterilized by soaking in a 1:1000 solution of zephyran. The tubing and the urinal are cleaned in the usual manner.

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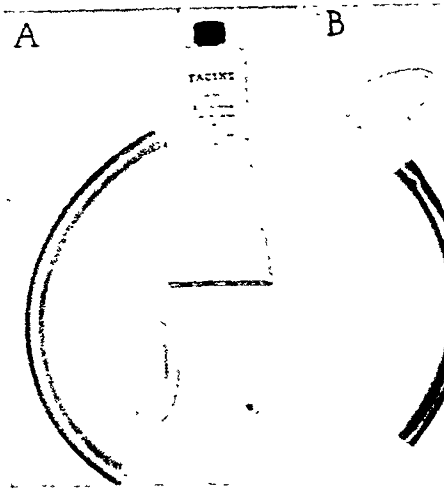

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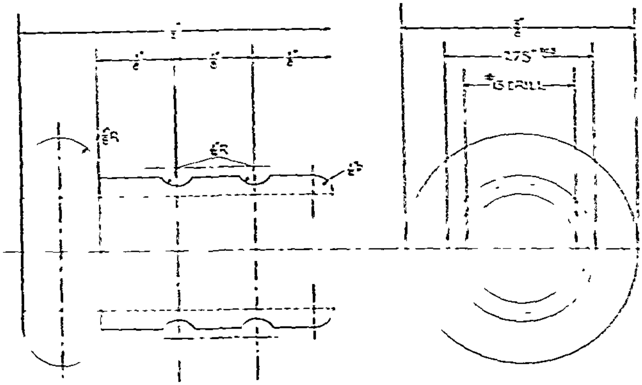

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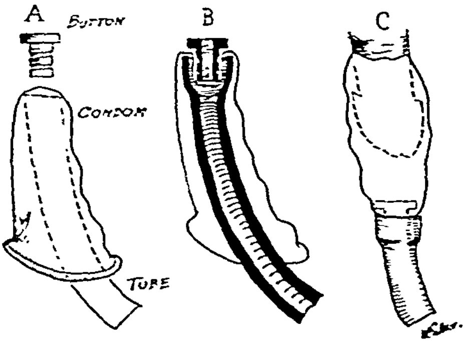

FIG. 3. *A*, inverted condom with adaptor about to be inserted. *B*, condom forced into tubing by adaptor. *C*, condom has been punctured, reversed and applied to penis.

and water. It may be sterilized by soaking in a 1:1000 solution of zephyran. The tubing and the urinal are cleaned in the usual manner.

SUMMARY

The use of a condom as a urinal coupling is not original but the general habit has been to fasten it to the penis with adhesive tape, with the disadvantages already mentioned. The use of cement obviates these while retaining the advantages of a disposable coupling. The other essential features of this apparatus are:

The plastic adaptor, with which a secure water-tight joint can be made in a few seconds. It is not yet in commercial production but can be made easily by anyone who can operate a machine lathe. The drawings are self-explanatory.

The precise size of the tubing, which has the effect of keeping the condom evacuated.

Since this article went to press, American Cystoscope Makers Inc., New York, N. Y. have announced that they will supply the plastic adaptor for this urinal.,

Portland VA Hospital, Sam Jackson Park, Portland, Ore.

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A PLASTIC HOLDER FOR NEPHROSTOMY TUBES

MORTON PALKEN

From the Urological Section of the Surgical Service, Cushing Veterans Administration Hospital, Framingham, Mass.

Experience with the usual unwieldy methods of securing nephrostomy catheters has prompted the designing of a plastic holder which may be found equally useful in holding drainage tubes in a variety of similar conditions.

The holder is simple to make, durable, and quite inexpensive. It consists of a rectangular shaped piece of acrylic plastic designed to provide a friction grip on the rubber tube (fig. 1). In order to provide adequate friction the hole (a) within the holder is made ten to twenty per cent smaller in diameter than the outside diameter of the tube. The tube is passed into the holder through the slot (b) after being placed on stretch to reduce its width (fig. 2).

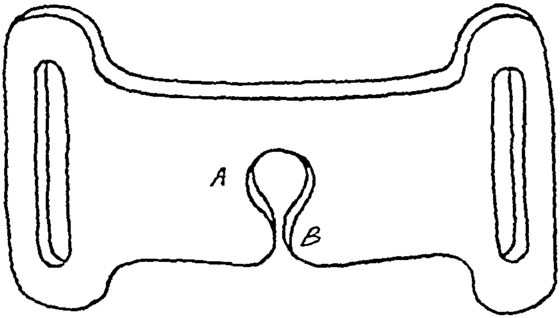

FIG. 1

Plexiglas in three-sixteenths of an inch thickness was found to be a satisfactory material. It is readily cut, drilled, and polished with ordinary tools, and can be easily shaped. The holder, after being heated in its midportion to about 300F (an alcohol lamp serves this purpose well), can be bent to fit the body contour and then fixed by cooling to room temperature under running water. It is applied to the body by a light elastic tape (fig. 3).

Because of the low melting point of Plexiglas the holders must be cold sterilized (e.g. by immersion for twenty four hours in one to one thousand aqueous solution of zephiran).

The device has been employed to hold catheters varying in size from 16 to 34F and has been particularly useful where permanent or long standing drainage tubes were in use.

My thanks are due to Mr. Bruno Tassinari of the Orthopedic Brace Shop in Cushing Veterans Administration Hospital, who was of great help in the development of this device.

Accepted for publication May 6, 1952.

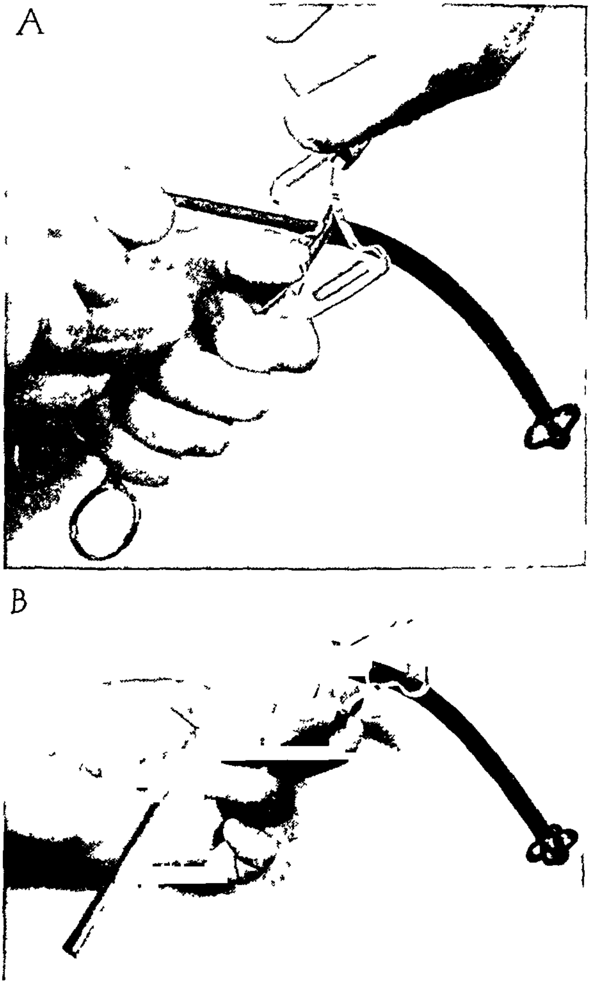

Fig 2

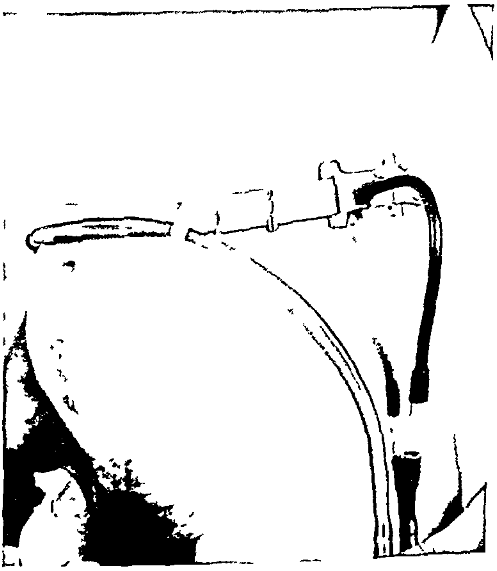

Fig 3

PROGRAM ANNUAL MEETING, SOUTHEASTERN SECTION AMERICAN UROLOGICAL ASSOCIATION, HOTEL NACIONAL, HAVANA, CUBA—MARCH 26, 27, 28, 29, 1953

MARCH 26

Horseshoe Kidney with Unilateral Pelvic and Ureteral Duplication and Ureteral Ectopia, Dr. John G. Menville, New Orleans, La.

The Effect of Estrogen on the Testes, Prostate, Adrenal and Pituitary of the Albino Rat, Dr. Kenneth M. Lynch, Charleston, S. C.

Plastic Operations for Hydronephrosis, Dr. F. E. B. Foley, St. Paul, Minn. (guest speaker)

T. Leon Howard Pyelogram Hour, conducted by Dr. Elmer Hess, Erie, Pa. (by invitation)

MARCH 27

Scientific Movies and Clinical Abstracts:

- Vertical Flap Ureteropelvioplasty, Drs. Peter L. Scardino and Charles L. Prince, Savannah, Ga.
- Phallectomy for Carcinoma and Gland Dissection, Dr. Leander W. Riba, Chicago, Ill. (by invitation)
- Conservative Surgery in Tuberculous Epididymitis, Dr. J. Robert Rinker, Augusta, Ga.
- Trilene in Urological Procedures, Drs. E. P. Alyea and V. A. Politano (by invitation) Durham, N. C.
- Control of Postoperative Kidney Incisional Pain, Drs. Linus W. Hewitt, Eugene S. Gilmer and Harold Carron (by invitation) Tampa, Fla.
- A Simplified Technique for Meatotomy of the Female Urethral Meatus, Dr. Norborne B. Powell (by invitation) Houston, Texas
- A Technique for Continuous Intermittent Irrigation of the Renal Pelvis, Drs. James H. Semans and Henry F. La Guette (by invitation) Atlanta, Ga.

The Management of Ureteral Calculi, Dr. W. E. Kittredge, New Orleans, La.

Pneumo-Retro-Peritoneo with Intravenous Pyelogram, Dr. F. Barquin, Habana, Cuba

Localization of Radioactivity in the Lymphatic Drainage of the Urinary Bladder Using Au-198, Drs. Avrom H. Isaacs, Harold F. Berg (by invitation) and William M. Christopherson (by invitation), Louisville, Ky.

Surgery of Pathological Conditions of the Adrenal Cortex, Dr. George F. Cahill (guest speaker) New York, N. Y.

Carcinoma of the Bladder, Dr. William M. Coppridge, Durham, N. C.

Ballenger Memorial Lecture: Acute Renal Failure, Dr. Homer W. Smith, New York, N. Y.

MARCH 28

Upper Urinary Tract Disease Associated with Urethral Stricture, Drs. J. Denny Moffett and David W. Goddard, Daytona Beach, Fla.

Present Conception of Retropubic Prostatectomy. Dr. Park Nicely, Knoxville. Tenn.

Contribution to the Study of the Differential Diagnosis of Cysts and Tumors of the Kidney, Dr. Luis F. Rodriguez Molina (guest speaker) Habana, Cuba

Symposium on Calculous Disease of the Kidney:

Newer Concepts Concerning the Physical Chemical Properties of Urine and their Relationship to Renal Calculous Formation, Dr. Joseph Seifter, Philadelphia, Pa. (guest speaker)

The Role of Infections in Calculous Disease of the Kidney, Dr. Elmer Hess, Erie, Pa. (guest speaker)

The Use of the Shorr Regime as a Prophylaxis Against Renal Phosphatic Calculi, Dr. Victor Marshall, New York, N. Y. (guest speaker)

Clinical Results in Patients Treated for Renal Calculous Disease with Hyaluronidase, Dr. Arthur J. Butt, Pensacola, Fla.

Past President's Address, Dr. Temple Ainsworth, Jackson, Miss.

ERRATUM

March 1953 issue, p. 455. Delete reference to footnote 4 in sixth line from bottom of page.

THE JOURNAL OF UROLOGY
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CHOLESTEATOMA OF KIDNEY SIMULATING SQUAMOUS CELL CARCINOMA

HANS N. NAUMANN AND SILVIO A. SABATINI

From the Veterans Administration Center, Jackson, Miss.

More than 100 years ago, Johannes Mueller designated as cholesteatoma a tumor of the brain composed of keratin lamellae of a mother-of-pearl sheen and cholesterol crystals. The term cholesteatoma is synonymous with "tumeur perlée" (Cruveilhier, 1829), "Perlgeschwulst" (Virchow, 1855), "pial epidermoid" (Bostroem, 1897) and also with epidermoid cyst (List, 1941). Besides the more common location in the brain and ear, cholesteatomas have occasionally been found in various sites such as the intestinal tract, genitalia, skin and eye. Another rare location is the urinary tract first described by Rokitansky in 1861. A distinction has been made between a true, genuine or primary cholesteatoma and a false or secondary one; the former denoting a true neoplasm such as in the brain apparently from anlage rests, while the latter refers to tumor-like heaping of keratin masses in body cavities such as the ear probably secondary to inflammation and squamous metaplasia. The following case exemplifies a cholesteatoma of the urinary tract with extreme changes of the kidney raising interesting clinical and pathological problems.

CASE REPORT

F. B .C., R- No. 26,566, a white man 54 years of age, was first seen January 8, 1950 with chief complaints of dull pain in the right upper abdominal quadrant, and in the right costovertebral angle of 1 month's duration. The pain would appear late in the day, and would disappear upon rest. The past history was irrelevant, except for an attack of gonorrhea in 1924 without sequelae. The patient stated that during the past 4 years he had been noting a "ropy" discharge at the beginning of urination. In November 1949, he had an episode of chills and fever for which he was hospitalized for 1 week elsewhere, and a diagnosis of pyelonephritis was made. Since that time, the patient has "felt tired and run down."

Physical examination revealed a well nourished, elderly, white man who was not acutely ill. The head and neck revealed no abnormal findings. The heart and lungs were negative; blood pressure 140/80. The abdomen showed nothing remarkable, except slight tenderness in the right upper abdominal quadrant. Digital examination of the rectum revealed a normal prostate. The musculoskeletal and nervous systems were intact.

A routine urine analysis was within normal range, as was a hemogram. The blood urea nitrogen was 16 mg. per cent, and a qualitative blood Kahn was negative. Phenolsulfonphthalein showed 35 per cent excretion in 1 hour, and a urea clearance test was 55 per cent of normal.

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cortical abscesses were exposed which measured up to 1.5 cm. in diameter and contained purulent and caseous material. The intervening surface was tan-whitish with gradual transition into a gray-tan, rather smooth surface at the middle and lower portions with scattered hemorrhagic and retracted areas. The medial aspect of the lower pole showed a cyst 1 cm. in diameter filled with brown fluid.

On bisection, the architecture of the upper two-thirds of the kidney was found to be entirely destroyed and replaced by a gray-white, fibrous tissue riddled and mottled by areas of caseation, measuring 1 to 10 mm. in diameter (fig. 1, *B*). After expressing some of the caseous material, there remained several cavities up to 2 cm. in diameter with partly smooth, partly necrotic walls. The architecture of the lower third of the kidney was fairly well preserved.

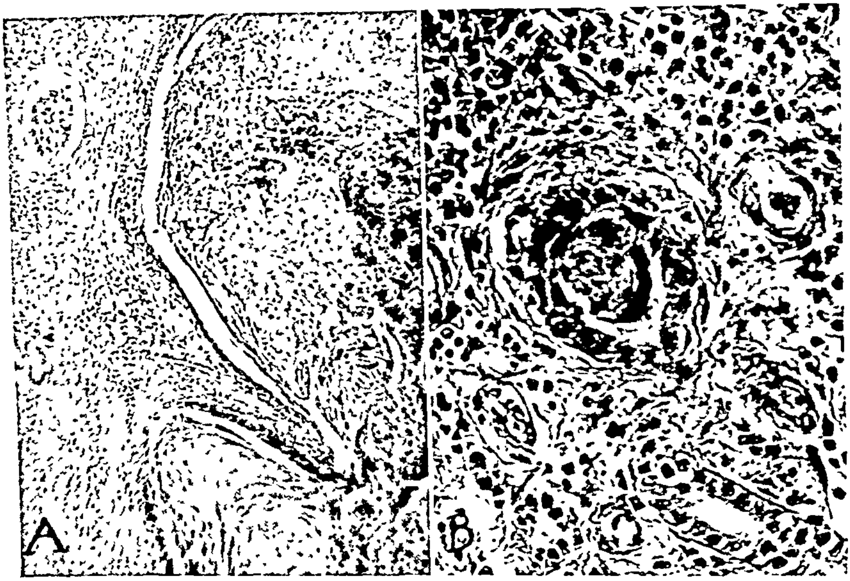

FIG 2 *A*, section from middle portion of kidney showing large cystic space lined by squamous cells and filled with keratin masses adjacent to parenchyma. × 35. *B*, section from medulla showing collecting tubule with squamous metaplasia and heaping of keratin. × 430.

The attached stump of the ureter measured 8 cm. in length and 1 cm. in diameter. The wall was 1 to 2 mm. in thickness and appeared infiltrated. The mucosa was white, partly smooth, partly rough and fissured and covered with purulent material. The pelvis showed similar changes as the ureter and blended into the mottled caseous areas of the parenchyma. The pelvic mucosa was likewise white, rough and covered with purulent material.

Microscopic examination of sections from the upper pole of the kidney showed masses of cystic tumor scattered throughout. The cysts varied from small round or ovoid structures to large spaces, all lined by stratified squamous epithelium and filled with cornified cells and amorphous keratin material in laminated arrangement (fig. 2, *A*). The squamous lining cells were mostly flattened and varied

An excretory urogram on January 9, 1950 was unsatisfactory for interpretation. A right retrograde pyelogram (fig. 1, *A*) was done on January 19, and showed no visualization of the right upper major calyx.

Culture of urine from the right kidney urine was negative for tubercle bacilli. A Papanicolaou stain of the sediment of the right kidney urine showed "cornified squamous epithelial cells with acidophilic cytoplasm, and also some transitional epithelial cells. These cells show no malignant characteristics."

X-ray examinations of chest, skull, femora and humeri were negative for metastatic lesions.

On January 24, the patient was taken to the operating room. Upon exposing the right kidney, the upper two-thirds were found to be enlarged, firm and nodular; therefore, a nephrectomy was performed, removing also the upper half of the right ureter. The patient made an uneventful recovery and was discharged on February 14. (See pathological report.)

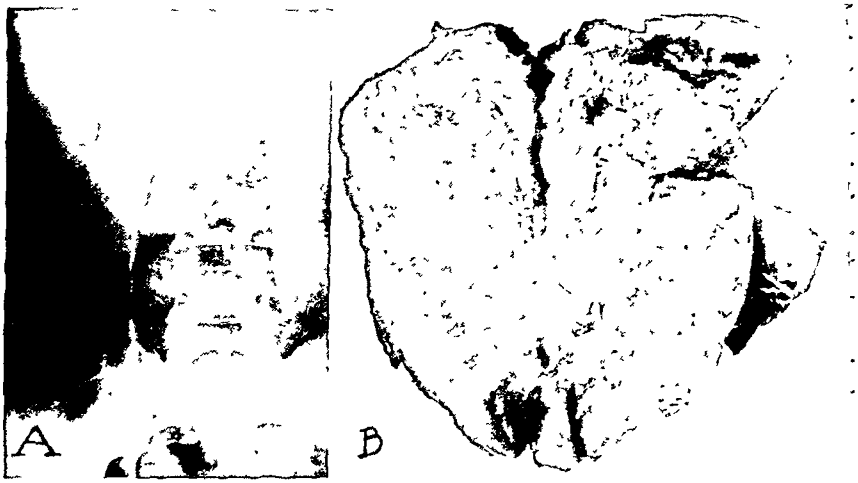

FIG 1 *A*, retrograde pyelogram of right kidney without visualization of upper major calyx. *B*, cut surfaces of bisected kidney showing destruction of upper and middle portions and replacement by caseous and purulent masses.

Follow-up examination (April 4, 1951): Patient stated that since his operation he had gained 30 pounds in weight and "feels like a new man."

Physical examination revealed a well nourished, ambulatory, adult male. Blood pressure 130/80. The abdomen and back showed a well healed right loin scar with no evidence of masses within the abdomen.

A routine urine analysis and a hemogram were within normal range.

A cystoscopic examination revealed a normal bladder with no evidence of tumefaction or hyperplasia of the mucosa. A left retrograde pyelogram was normal, but a Papanicolaou stain of the left kidney urine showed numerous squamous cells.

Pathological report: The gross specimen was a right kidney measuring 15 by 8 by 6 cm. and weighing with part of the capsule 409 gm. The latter was red, congested and thickened by infiltration to 1.3 cm. at the upper pole. It stripped with ease at the lower pole, but with difficulty at the upper two-thirds. Multiple

DISCUSSION

On perusing the accessible literature, we were able to find only very few reports of cholesteatomas of the urinary tract. A comprehensive study of this subject by Kuettner appeared in 1919 and lists 19 case reports including one by that author; but only six were actual cases of cholesteatoma while the remainder presented cholesteatoma-like features in cases of squamous cell carcinoma or of extensive leukoplakia of the urinary tract. In 1930, Immink reported 2 cases of which only the first, in our opinion, fulfills the criteria of a cholesteatoma. Another case was reported by Bruegel in 1934. The important data of these 8 cases from the literature and of the one presently reported are summarized in the following abstracts.

ABSTRACTS OF NINE CASES OF CHOLESTEATOMA OF THE URINARY TRACT ARRANGED CHRONOLOGICALLY

1) Lowenson: Petersburger med. Ztschr. 1862, p. 225 (quoted by Kuettner). A 40 year old woman who died of purulent peritonitis was found at autopsy to have a hugely distended bladder lined by thick cornified epithelium and filled by desquamated masses of grains and glistening scales which weighed 3¾ pounds and contained much fat.

2) Beselin: Virchow's Arch. 99: 289, 1889 (quoted by Kuettner). A 35 year old man had, for 5 years, renal colic and excretion of membranous shreds weighing an estimated 1000 gm. in all. Findings included a round, hard mass in the right lumbar region and presence of pus, cholesterol crystals and glistening lamellae in the urine after colics. During right nephrectomy the tightly filled pelvis ruptured spilling pus and white lamellae, and death occurred 8 days later. Autopsy revealed a cholesteatoma of the pelvis with leukoplakia and tuberculosis of right kidney and ureter, cystitis and peritonitis.

3) Hallé, Annales des mald. d. org. génito-urin., obs. I, p. 484, 1896 (quoted by Kuettner). A 39 year old man with cystitis and ureteropyelitis for 17 years died after curettage of bladder. At autopsy there were large cholesteatomatous, cheesy masses in the left renal pelvis and ureter above a stenosis, and leukoplakia of the entire urinary tract except the urethra.

4) Bruechanow: Prager med. Wchnschr. No. 42 and 43, 1898 (quoted by Kuettner). A 36 year old man was suffering with bladder trouble for 22 years and had been operated for bladder stone twice unsuccessfully. Necropsy revealed a cholesteatoma of the bladder forming white pasty masses, leukoplakia of bladder and ureters, right pyelonephritis, left nephrosclerosis, and lobular pneumonia.

5) Fulci: Lo Sperimentale 1909. Abstr. Barbacci: Zentralbl. f. allg. Path. and Path. Anat. 21: 266, 1910 (quoted by Kuettner). A cholesteatoma of a hydronephrotic sac is described forming concentric lamellae of mother-of-pearl appearance and containing cholesterol and fat. There was also leukoplakia and neprholithiasis. (No data on age or sex are available.)

6) H. Kuettner: Bruns Beitr. 114: 609, 1919. A 35 year old man had a vesical fistula following a bullet wound and pyonephrosis. The right kidney was reslightly in size, shape and staining reaction with few mitotic figures. Some of the smaller cell masses were solid resembling pearl nests, others showed beginning central degeneration of the cell clusters, thus forming a transition to the large, more thin-walled cysts.

Sections from the lower pole showed degenerative changes of the parenchyma such as capsular edema, tubular degeneration, lymphocytic infiltrate, calcium deposits and compression of tissue around the cystic spaces. Sections of pelvis showed stratified squamous lining with moderate variation in size and shape of cells. The basal layer was sharply demarcated, but there were some down-growing pegs composed of more irregular and hyperchromic cells. The ureter showed a similar squamous lining with some hydropic degeneration. The wall was infiltrated with plasma cells and lymphocytes. The capsule showed a thick layer of fibrous tissue with collections of plasma cells. Scattered in places were needle-shaped spaces indicating cholesterol crystals surrounded by numerous foreign body giant cells. The periphery showed fat and an area of adrenal tissue.

Diagnosis: The first impression was that of a low-grade squamous cell carcinoma of the pelvis on the basis of the resemblance of the many small cysts with pearl nests, of the scattering of these cysts through the parenchyma, appearing like invasion, of the slight cell atypism and the extensive leukoplakia generally considered a precancerous lesion. However, it was felt that this interpretation was not entirely satisfactory, because the histological criteria of malignancy were indefinite and the process, instead of an invasion of the subepithelial tissues, was, on the contrary, an outgrowing hyperkeratosis and desquamation resembling that of a benign epidermal cyst. Furthermore, a strong point against malignancy was absence of capsular invasion, although conditions for such invasion appeared favorable due to the strong adherence of the capsule and its close contact to the parenchyma as evidenced by the extension of inflammation and of foreign body reaction to cholesterol, evidently derived from the cortical cyst contents.

In the course of the investigation, topographic sections of the entire kidney were prepared by the Armed Forces Institute of Pathology; and, from these sections after a more detailed study the diagnosis of cholesteatoma of the kidney became apparent, an interpretation agreed upon also by the staff of the Institute. The examination of the topographic sections revealed that the squamous metaplasia was much more widespread than anticipated and involved not only the ureter, the pelvis and the calyces, but extended even into the tubular system of the kidney. Many of the collecting tubules showed various stages of metaplasia varying from partial to complete replacement of the tubular epithelium by squamous cells (fig. 2, *B*). The production of keratin in confined spaces, then, resulted in cyst formation analogous to that of epithelial or epidermoid cysts in other parts of the body. On the basis of these findings it was concluded that what previously appeared to be an invasion of the parenchyma by squamous cells, was in reality a squamous metaplasia of renal tubules with subsequent accumulation of keratin and cyst formation characteristic of a cholesteatoma which occupied the parenchyma as well as the pelvis.

chemical composition such as varying fat and water contents. The resemblance with tuberculous caseation can be so striking, as in the present case and that of Immink (abstracts of cases 7, 9), that bacteriological examinations for acid-fast organisms were done. On the other hand, tuberculosis may be a complicating factor (abstract of case 2) and bacteriological studies in cholesteatoma of the kidney may, therefore, be indicated.

A clinical diagnosis of cholesteatoma of the upper urinary tract can not be expected to be made, unless cholesteatomatous membranes are expelled in the urine as in the case of Beer and of Beselin. On the other hand, the appearance of flakes and shreds in the urine have been observed in leukoplakia. In other cases squamous cells were found only microscopically and in the present case still were present in the urine of the remaining left kidney. It may, thus, be concluded that the presence of squamous cells in catheterized urine, microscopically or macroscopically, can indicate leukoplakia, cholesteatoma or squamous cell carcinoma. Pyelographic changes may help to narrow the differential diagnosis although the possibility of a concomitant lesion such as tuberculosis must be borne in mind.

SUMMARY

A case of cholesteatoma of the kidney is presented with extreme leukoplakia of pelvis, calyces, collecting tubules and ureter and cholesteatomatous changes within the parenchyma and pelvis. The clinical and pathological features have been discussed.

We wish to express our gratitude to the Armed Forces Institute of Pathology, in particular, to the Director, Brigadier General Elbert De Coursey, and to Dr. F. K Mostofi, for their interest and help.

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moved and showed a massive cholesteatoma of the pelvis which was lined by granulation tissue.

7) *E. A. Immink: Nederl. Tijdschr. Geneesk. 74: 3012, 1930.* A 45 year old man suffered for 12 years of renal colic, dysuria, hematuria and on cystoscopy showed swelling of the right ureteral ostium preventing catheterization. After right nephrectomy a cholesteatoma of the pelvis with yellow-white crumbling masses, leukoplakia and pyonephrosis was found.

8) *F. S. Bruegel: Wien. med. Wchnschr. 41: 1097, 1934.* A 36 year old man had renal colic 9 years ago and recently, on excretory urography, showed incomplete filling of the left pelvis. By left pyelotomy a large cholesteatoma was removed consisting of atheromatous masses of cornified epithelium.

9) *Present authors.* A 54 year old man had renal pain of 1 month's duration and on pyelography showed a filling defect of the right upper calyx and cornified squamous cells in the right kidney urine. After nephrectomy examination of the specimen revealed caseous masses in pelvis, calyces and parenchyma as well as extensive leukoplakia of the urinary tract involving also the collecting tubules.

Although we realize that 9 cases is an insufficient material for statistical analysis, we think, nevertheless, that the following conclusions may be drawn tentatively regarding urinary tract cholesteatomas: 1) There is a preponderance of males (7 males, 1 female). 2) The main age incidence is between 35 and 45 years (7 cases). 3) The favored localization is the renal pelvis (6 cases). 4) A concomitant chronic inflammation is present in the majority (7 cases).

The unique feature of the present case is the extension of the cholesteatomatous changes from the pelvis into the ductal system of the parenchyma simulating squamous cell carcinoma as described above. This is an illustration of the difficulties which may be encountered in differentiating cholesteatoma, squamous metaplasia and squamous cell carcinoma. There may be the possibility of malignant degeneration in a cholesteatoma suggested by the description in the literature of cases of cholesteatoma or cholesteatoma-like lesions which were proven to be squamous cell carcinomas by the presence of metastases.

Regarding the etiology, Kuettner postulated two prerequisites for cholesteatomas of the urinary tract: leukoplakia and impaired urinary drainage. Although squamous metaplasia of small areas in chronic cystitis or at urethral strictures is a rather common finding, large areas of leukoplakia of the urinary tract appear rare enough to be the subject of a number of reports (see references). The second prerequisite, impaired drainage, is self-evident, since accumulation of keratin masses can not result if washed away by the urine. A narrowing of the ureter by leukoplakia may be one of the causes of impaired drainage in some cases.

The gross appearance of urinary tract and other cholesteatomas has been described in two different ways. The classical description is that of pearly white lamellae. A number of cholesteatomas including the present case contain caseous, cheesy, pasty or atheromatous masses (abstracts of cases 3, 4, 6, 9), which apparently answer the description of contents of sebaceous or epithelial cysts of the skin. The cause of the different appearance is obviously due to differences in no complaints. He gave the following history: Two days before coming to the hospital he had fainted while shaving. He consulted his family physician who after examination informed him that he had an abdominal tumor and should be hospitalized. The patient had been unaware of the abdominal mass and, until he fainted, considered himself to be in good health. There was no history of weight loss, pain, nor weakness. His appetite was good, and he had had no symptoms referable to the genito-urinary tract. The only positive finding we were able to elicit from his history was that he recalled having passed a blood stained stool 6 weeks previous to admission.

Physical examination was not remarkable. He appeared in general to be a healthy, slightly obese 55 year old man. The heart and lungs were normal. The blood pressure was 154/84. Inspection of the abdomen with the patient in the dorsal recumbent position disclosed an ovoid mass elevating the left flank and extending slightly past the midline to the right. The abdominal veins were slightly more prominent than usual. Palpation revealed the mass to be non-tender, smooth, and freely movable. It was firm but had a somewhat cystic quality when compressed. It appeared to occupy the entire left flank and to extend to the right past the midabdominal line. There was no evidence of embarrassed venous return such as varicocele, varicose veins, or hemorrhoids. The external genitalia were clinically normal, as was the prostate.

Urinalysis was normal. Smear and culture were negative. Other laboratory studies were within normal limits: red blood cells, 4.7 million; hemoglobin, 75 per cent; nonprotein nitrogen, 23.4; phenolsulfonphthalein 30 per cent excretion the first hour, 25 per cent excretion the second hour.

X-rays: Chest films negative. Barium enema negative except for lateral and anterior displacement of the colon due to a retroperitoneal mass. Excretory urography, good bilateral function. Filling of the left pelvis was distorted due to compression of lower pole.

Cystoscopy on February 14 disclosed a normal bladder and prostatic urethra. The ureters were easily catheterized. About 40 cc of clear urine was obtained from the left kidney when catheterized. Skiodan (30 cc of 20 per cent solution) was instilled into left kidney without discomfort. Retrograde pyelogram disclosed compression of pelvis and lower calyces (fig. 1, *A*) by a mass at the lower pole. The outline of the mass was plainly visible on several preceding and subsequent films of the abdomen. An aortogram (fig. 1, *B*) disclosed branches of the renal artery coursing about the mass. The tumor for the most part was avascular. The latter fact influenced us in making a clinical diagnosis of cyst of lower pole of left kidney.

Because of a history of bloody stools, the patient was sent to the proctology clinic February 20, where a small rectal polyp was found and removed. This was reported as a benign polyp by the department of pathology.

On February 23, under a general anesthetic of sodium pentothal, nitrous oxide and ether, the left retroperitoneal area was exposed through a curved lumbar incision. The peritoneum was only slightly adherent to the mass and was easily

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FIBROSARCOMA OF THE ADULT KIDNEY: CASE REPORT

T. EUGENE RUFF

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Before 1910 little effort was made to classify renal tumors accurately. Prior to that time, carcinoma of the kidney was often classified as sarcoma. Then, too, it has only been in the last 20–30 years that the service of well trained pathologists has been available to hospitals through out the country. Consequently, in recent years tissue removed at operation is more carefully studied. Due to the aforementioned facts, we find a paucity of case reports of fibrosarcoma in recent literature. In 1948, Culp and Hartman[1] published an excellent article dealing with adult renal tumors. In their review of the literature, they found that adult type embryonal tumor of the renal cortex had been reported with more than fifty different pathological diagnoses. Obviously, the resulting confusion makes one skeptical of the accuracy of diagnosis in some of the previously reported cases of fibrosarcomas of the kidney. Despite the many attempts in recent years to classify renal tumors, there is still no universally accepted nomenclature in their classification. In general, renal sarcomas have been subdivided by their microscopic picture into fibrosarcoma, myosarcoma, liposarcoma, osteoblastic sarcoma and undifferentiated.

Mintz[2] reviewed the literature in 1937 and was able to find only ninety three well authenticated cases of renal sarcoma. This group was made up of cases reported between 1910 and 1937 and excluded any patient under 21 years of age. Of the 93 cases which he studied, only fifteen were fibrosarcoma. A further example of the infrequency of this tumor is the fact that Judd and Donald[3] in reporting on a series of 570 operations at Mayo Clinic for renal neoplasms found only six fibrosarcomas.

Moore[4] reported a case of renal fibrosarcoma in 1951. After reviewing the literature he concluded that this was the one hundred and third reported. The writer was able to find only approximately sixty such case reports. However, only those cases reported since 1910 have been included in the present report.

Since this tumor, though uncommon, is of pathological interest and because of the associated diagnostic problem, the following case is presented.

CASE REPORT

S. F. R. (Hospital No. 49459), a 55 year old white male social worker, was admitted to the hospital on February 9, 1951. At the time of admission, he had

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[1] Culp, O. S. and Hartman, F. W.: Mesoblastic nephroma in adults: A clinicopathologic study of Wilms' tumors and related renal neoplasms. J. Urol., 60: 552–576, 1948.

[2] Mintz, E. R.: Sarcoma of the kidney in adults. Ann. Surg., 105: 521–537, 1937.

[3] Judd, E. S. and Donald, J. M.: Sarcoma of the kidney of the adult. Ann. Surg. 96: 1028–1031, 1932.

[4] Moore, T. D.: Unusual renal tumors. J. Urol., 66: 533–546, 1951.

no complaints. He gave the following history: Two days before coming to the hospital he had fainted while shaving. He consulted his family physician who after examination informed him that he had an abdominal tumor and should be hospitalized. The patient had been unaware of the abdominal mass and, until he fainted, considered himself to be in good health. There was no history of weight loss, pain, nor weakness. His appetite was good, and he had had no symptoms referable to the genito-urinary tract. The only positive finding we were able to elicit from his history was that he recalled having passed a blood stained stool 6 weeks previous to admission.

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The following in brief is the reported findings of the pathology department.

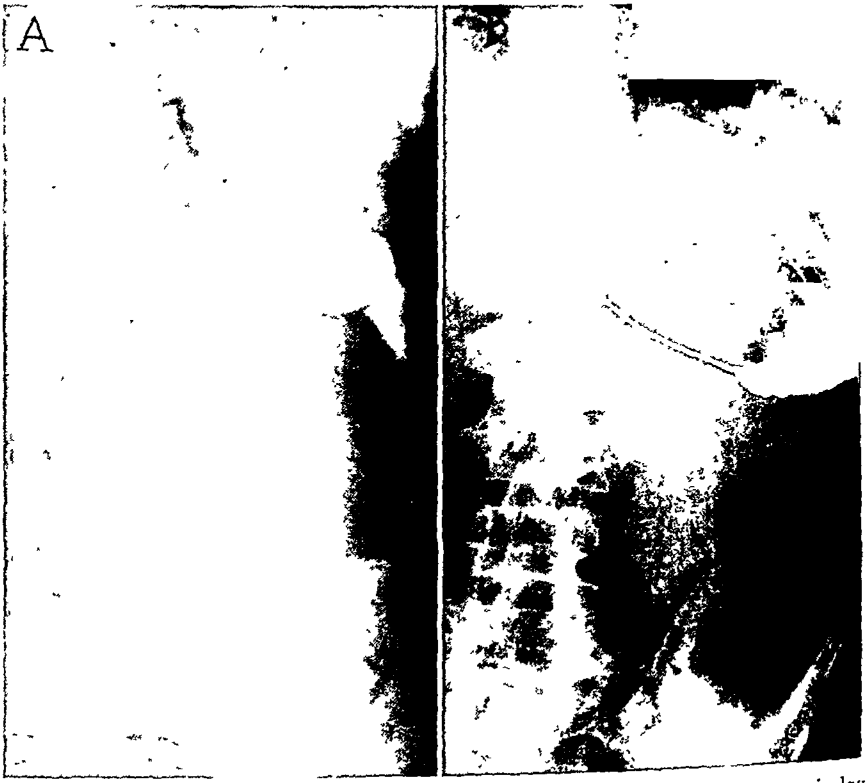

FIG. 1. *A*, retrograde pyelogram disclosed compression of renal pelvis by mass in lower pole. *B*, aortogram. Note superficial vessels surrounding mass.

"The combined weight of the kidney and tumor is 1340 gm. The tumor is firm but rubbery with a light yellow capsule. It cuts similar to a uterine fibroid. The cut surface (fig. 2) is composed of nodular masses of grayish white and yellowish green areas. There are some cystic areas. The tumor is from the lower pole of the kidney close to the renal pelvis and compresses the proximal ureter. The renal pelvis and major calyces are dilated.

"Microscopic section (fig. 3) discloses the tumor to be made up of spindle shaped stromal cells growing in groups or bundles and forming a variable amount of intracellular hyaline. The tumor cells vary somewhat in size, staining reaction and degree of differentiation. Some are growing into an imperfectly formed capsule. Compressed renal tubules are present within the tumor proper as well as

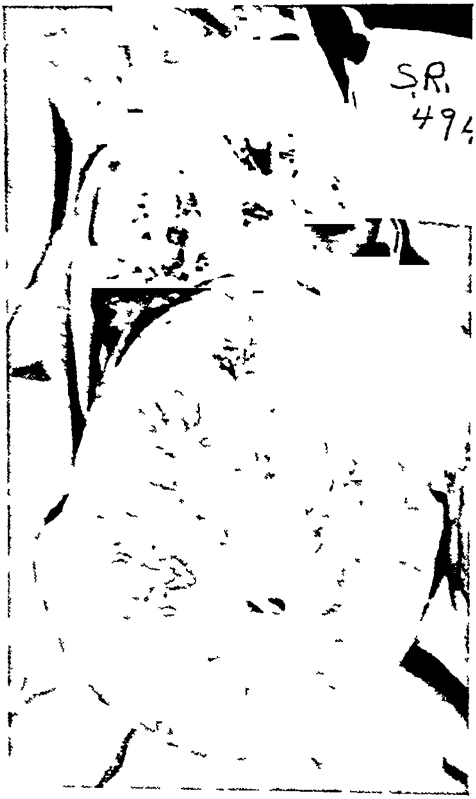

Fig 2 Kidney with attached tumor

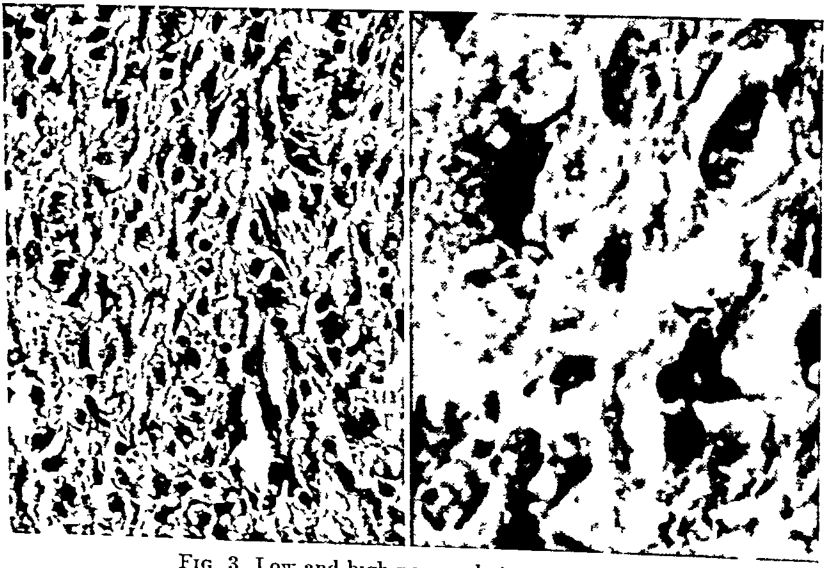

Fig 3 Low and high power photomicrographs

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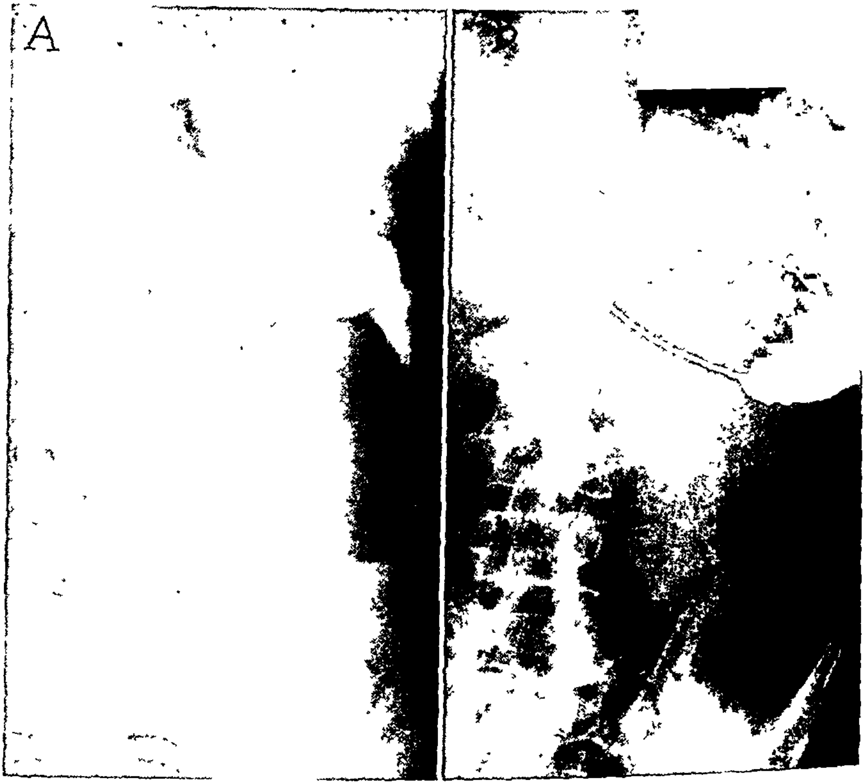

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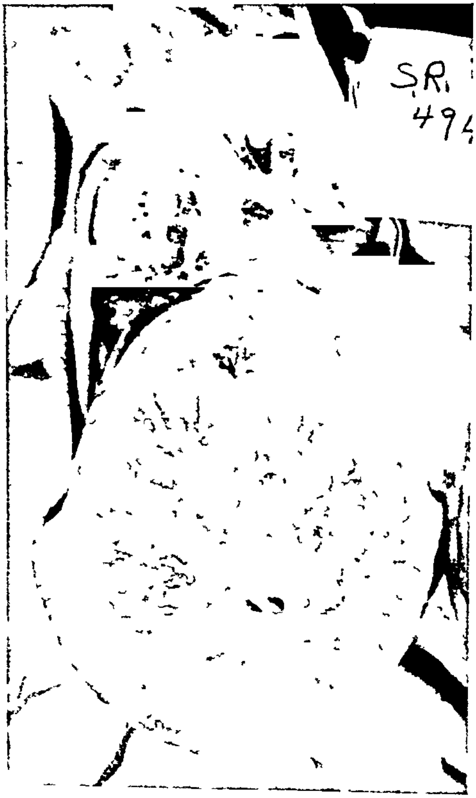

FIG 2 Kidney with attached tumor

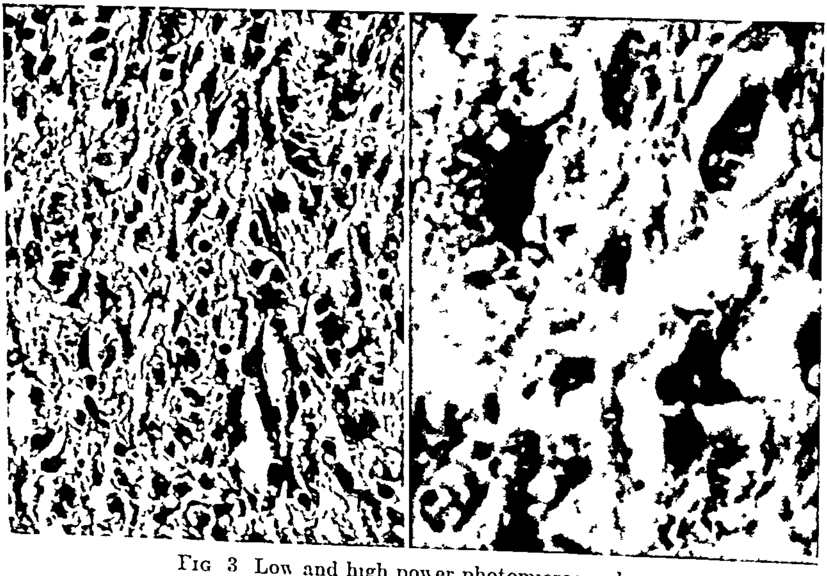

FIG 3 Low and high power photomicrographs

at its periphery. There are some abnormal mitosis. Tumor giant cells are present. There is considerable variation in morphology and degree of cellularity of the tumor cells. Final diagnosis: Fibrosarcoma arising from fibroma in kidney." Signed, Harold Gordon, M.D., Chief, Laboratory Services.

The patient did well following surgery until his second postoperative day when marked atelectases of right lung developed. Bronchoscopy was done and a large amount of fluid was aspirated. Convalescence thereafter was uneventful.

The patient has been seen in follow-up clinic at intervals of 3 months since surgery. His last follow-up visit was a year after the nephrectomy. At this time, there was no clinical evidence of local nor distant metastasis. X-ray studies of chest and abdomen were negative. The patient had no complaints. He is currently on a reducing diet because of a weight gain of 20 pounds during the past year.

DISCUSSION

Renal sarcoma, although rare in the adult kidney, must be considered in differential diagnosis of retroperitoneal tumors. There are no clinical features which are diagnostic. A large percentage of previously reported cases have had colicky pain with or without hematuria. Eighty per cent have the physical findings of a palpable mass. The above case is unusual in having been completely asymptomatic. Of the previous case reports reviewed, only one was asymptomatic. This one was reported by McNamara, Smith and Gore[5] and was discovered when the patient was operated for tumor of the cord. The cord lesion was found to be of metastatic nature from renal fibrosarcoma.

The point of origin is controversial. In some cases, the tumor is thought to arise from the renal capsule.[6] In others, it apparently originates from the connective tissue of the kidney parenchyma as suggested by Weisel, Dockerty and Priestley.[7] Treatment of this tumor, as with most neoplasms, consists of early discovery and radical removal. Postoperative radiation is of doubtful value. It was not given in our case.

Prognosis, despite treatment, is always poor. We are cautiously hopeful for the above case since there was no evidence of extension through the capsule and microscopically it was of low grade malignancy. These tumors apparently infiltrate before distant metastases occur.[8] There is, however, the ever present danger of implants and venous thrombi at the time of surgery. Of the fifteen cases reported by Mintz,[2] only one was living six years and three months after surgery. Weisel, Dockerty, and Priestley[7] give a slightly more favorable report on their series, one case being alive eleven years later. They conclude that 10 per cent of the patients operated upon survive 5 years.

[5] McNamara, W. L., Smith, H. D. and Gore, W. A.: Symptomless renal fibrosarcoma with spinal metastases. Am. J. Clin. Path., 10: 343, 1940.

[6] Powell, T. O. and Clark, J. E.: Renal sarcoma. J. Urol., 62: 751–755, 1949.

[7] Weisel, W., Dockerty, M. B. and Priestley, J. T.: Sarcoma of the kidney. J. Urol., 50: 564–573, 1943.

[8] Armstrong, C. P.: Fibrosarcoma of the kidney. J. South Carolina Med. Assoc. 46: 155–158, 1950.

CONCLUSIONS

A case of fibrosarcoma of the adult kidney is presented.

Approximately sixty authentic cases of such tumors have been reported since 1910.

The tumor in this case was asymptomatic.

Postoperative radiation was not given.

In the twelve months since surgery, the patient has gained twenty pounds, and there is no evidence of recurrence of the tumor.

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RENAL ADENOMA. PYELOGRAMS SHOWING THE GROWTH OVER A FIVE YEAR PERIOD

HARRY S. SHELLEY

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Adenomas of the kidney are not uncommon; most are small, non-symptom producing and found incidentally at the autopsy table. Adenomas which produce symptoms are not so common. Cristol, Bothe and Grotzinger, in 1949, collected 49 cases in a review of the literature and presented one of their own.

This case is being reported because of the unusual opportunity of presenting roentgenograms taken 5 years apart which show the progress of the adenoma.

CASE REPORT

H. D., a white man, aged 52, reported to the hospital in October 1950, complaining of intermittent painless hematuria, which had been present for 6 years. Pain, burning or discomfort were not associated with the bleeding. This was at no time a terminal hematuria, but the whole specimen would be stained. It might be only one specimen, or it might be each one for several days. The intervals at which the hematuria appeared varied considerably, the longest interval being 3 months. The patient had no other urinary symptoms. He gave no history of tuberculosis; but there was a history of duodenal ulcer which had been present for about 10 years and had improved on a medical regimen with occasional flare-ups, the last of which occurred within the year with a loss of about 15 pounds in weight. He also gave a history of lues in 1917 for which he had received a fairly long course of salvarsan.

When he was admitted to this hospital his physical examination was negative except for an unexplained variation in the blood pressure, right arm being 150/90 mm. of mercury, left arm 120/80. There were no palpable masses in the abdomen, and both kidneys could be felt and gave the impression of being normal in size. Laboratory examinations were as follows: WBC 10,600, hemoglobin 13 gm., PCV 47. Urine showed 30–35 RBC and a trace of albumin. Wassermann reaction and Kahn were negative. The nonprotein nitrogen was 41 mg. per cent. Bladder culture showed Staphylococcus aureus, probably a contaminant. Acid fast cultures taken at this time did not show any growth at the end of 6 weeks. Papanicolaou stains and studies of the catheterized specimens from each kidney revealed only "desquamated epithelial cells of normal morphology. No tumor cells were identified." The patient had been seen in another hospital in 1945 when a roentgenogram (fig. 1, *A*) was taken. Nephrectomy was advised at this time but the patient refused. Retrograde studies were made on this present admission and the pyelogram (fig. 1, *B*) was obtained showing an increase in the filling defect and the caliectasis; the infundibulum had become kinked.

Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The Statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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Various diagnoses were considered: papilloma of the lower right calyx; blood clot possibly from a small hemangioma of the calyx; non-opaque stone; calycine cyst due to an abscess formation; localized caliectasis. All of these possibilities had many faults and discrepancies and really very little evidence to support any one diagnosis. Adenoma was not considered. Nephrectomy was advised and accepted.

On October 6, 1950 a right nephrectomy was done through the usual flank incision. No difficulties were encountered and there were no marked adhesions or extension of the growth beyond the kidney. The specimen removed was about 10 by 5.5 cm. with a knob-like projection 3 cm. in diameter just above the lower pole. Weight was 155 gm. Cross-section of the organ (fig. 2) showed the knob-like projection to be a soft, opaque, yellow tumor mass measuring 4 by 1.5 cm. and, as can be seen, projecting into the calyx.

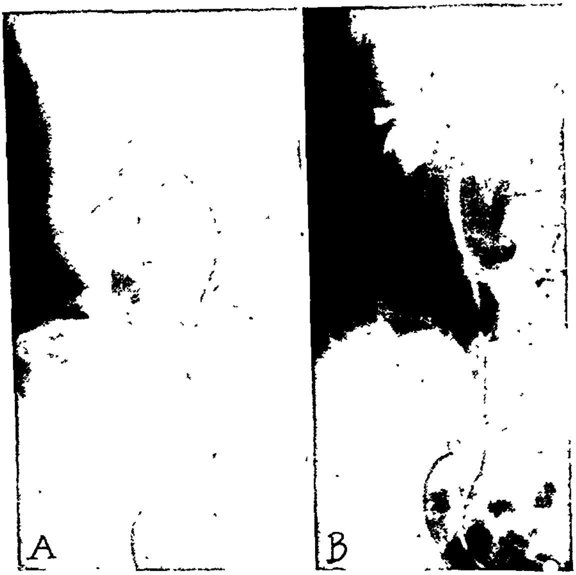

FIG. 1

Microscopic findings (fig. 3), as described by Dr. Maurice Wilson, are as follows: "The tumor in the lower pole of the kidney is composed of a tangle of small, well differentiated tubular channels which are, generally, lined by small cuboidal cells of quite uniform morphology; however, in many places this epithelium has been converted into large pale-staining foam cells which fill and distend the neoplastic tubules. Areas of necrosis, islands of condensed and partly mineralized fibrous stroma, small cystic cavities filled with amorphous material containing acicular slits from cholesterol crystals, and fresh hemorrhages are scattered throughout the tumor. This neoplasm appears to be very well delimited, even though a portion of it projects into the renal pelvis. The intact portion of the kidney shows no striking microscopic abnormalities. Some tubular atrophy and interstitial lymphocytic infiltration are noted in the vicinity of

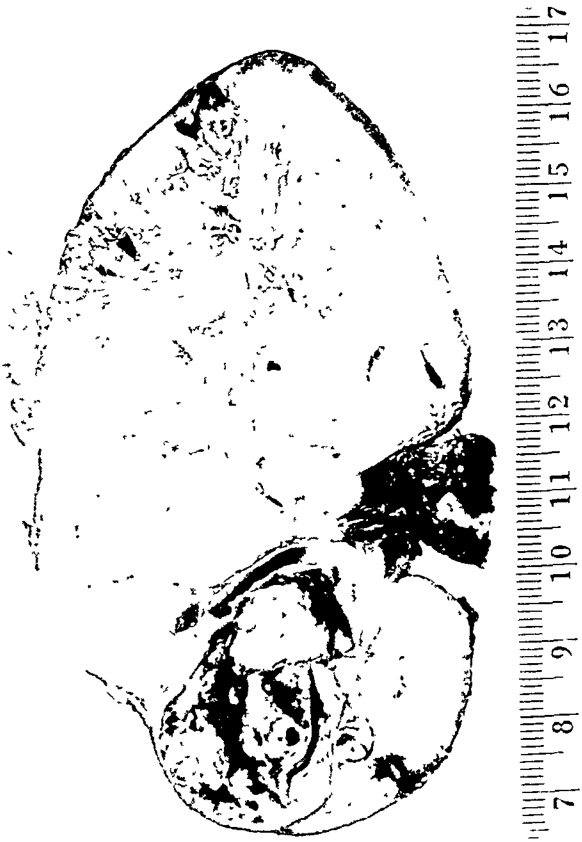

FIG 2

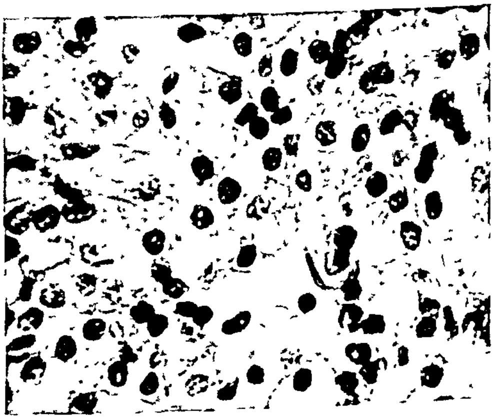

FIG. 3

the tumor where the parenchyma has been compressed and the pelvic mucosa displays rather heavy subepithelial infiltration with lymphocytes, plasma cells and a few eosinophils.—The microscopic structure of this neoplasm, as well as its seemingly very limited invasive properties suggest that it represents a tubular adenoma rather than a renal cell carcinoma. Diagnosis: Kidney: Adenoma."

The wound healed readily and convalescence was uneventful. The patient was discharged on the twelfth postoperative day. He was seen one year later, had gained 40 pounds, and was feeling quite well.

SUMMARY

A case is described in which pyelograms taken 5 years apart show the growth of a renal adenoma into the calyx and the changes produced in the kidney. The patient had intermittent hematuria over this period of time.

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RENOCOLIC FISTULA: REPORT OF A CASE

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This uncommon lesion was originally described by Hippocrates in the 5th century B.C., and clearly discussed by Rayer in 1841. We wish to add another case to the 49 previously recorded in the literature.

CASE REPORT

J. W. S. (GH 23029), a 56 year old white male electroplater, was admitted to the Veterans Administration Hospital, Los Angeles, Calif. on March 5, 1951 complaining of intermittent left flank pain for the past 5 years. In 1930 the patient first had pain in the left flank which was diagnosed and treated as "spastic colitis." He was then asymptomatic until 5 years ago at which time he had an attack of pain in the left costovertebral angle severe enough to cause syncope. His pain ceased within a few days and he was then well except for occasional similar episodes occurring every 2 to 3 months. These attacks usually lasted about 1 day and were often initiated by constipation. There was a 15 pound weight loss during the past year. His past history and systemic review were noncontributory.

Upon admission his temperature was 98.8F, pulse 100 and respiration 20. His blood pressure was 130/70. There was slight tenderness in the left flank of his abdomen and the liver extended 2 cm. beneath the right costal margin. Peristalsis was active. The remainder of the physical examination was normal.

Urinalysis: Specific gravity 1.005, albumin and sugar negative, occasional hyaline cast and white blood cell. Blood: Red blood cells 3,300,000, hemoglobin 10.9 gm., white blood cells 19,700, neutrophils 55 per cent, lymphocytes 31 per cent, monocytes 5 per cent and stab forms 9 per cent. Blood Wassermann reaction was negative. X-ray examination of the chest showed miliary concretions scattered through both lung fields which were interpreted as a healed miliary tuberculous infection. An excretory urogram showed normal right kidney function with absence of excretion of the dye on the left. A large staghorn calculus was present in the left kidney area. A barium enema revealed extravasation of the barium from the colon, just distal to the splenic flexure. No intrinsic lesion of the colon could be found. An upper gastro-intestinal series with study of the small bowel was normal. The lower bowel was normal when examined through the sigmoidoscope to 25 cm. The left ureteral orifice could not be visualized at cystoscopy, although the remainder of the bladder appeared normal.

Laparotomy was performed using an upper abdominal transverse incision. The splenic flexure of the colon was found to be intimately adherent to the lateral

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and anterior surface of the left kidney. This organ was about one and a half times the size of the normal right kidney. The remainder of the abdominal organs were not remarkable. The left kidney and the splenic flexure of the colon were removed en masse. Continuity of the bowel was re-established by open end-to-end anastomosis between the transverse and descending colon. The lower end of the ureter was ligated. A drain was brought through a separate wound in the left flank.

Parenteral fluids, electrolytes, penicillin and streptomycin were given in the postoperative period. The patient was ambulatory on the day following surgery, and liquids were given by mouth on the second postoperative day. His temperature was normal for the first nine postoperative days, following which he had daily elevations to 101F for 10 days accompanied by pain in the left flank. No drainage occurred from the wound, and the fever and flank pain gradually subsided. He was discharged from the hospital 27 days after the operative procedure.

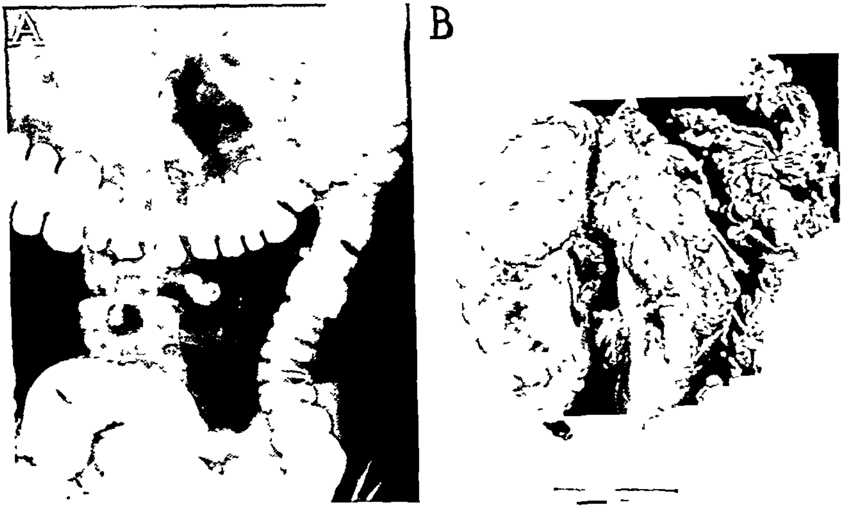

FIG. 1. *A*, barium enema showing extraluminal barium in left upper quadrant. *B*, resected kidney. Calculus can be seen in pelvis and parenchyma is replaced by adipose tissue

Examination of the specimen removed at surgery revealed that the kidney parenchyma had been largely replaced by adipose tissue. The renal pelvis contained a large staghorn calculus and the pelvic mucosa was extensively ulcerated and necrotic. Two fistulous tracts extended between the kidney pelvis, through the kidney substance, to the colon. There was tuberculoid reaction in the wall of the fistulous tract, but no tubercle bacilli could be found. Although many foreign body giant-cells were present, it was the opinion of the pathologist that tuberculosis was not the underlying disease.

DISCUSSION

Findlay in a review of the literature found that all recorded cases of renocolic fistula had their origin primarily in the kidney. There were none in which the fistula was believed to be secondary to disease of the colon. Wesson found no instance of renocolic fistula following malignant disease. Ratliff and Barnes, in a study of 37 cases, found that the fistula resulted from renal calculi associated with infection in 14, inflammation without calculi in 18, and only 5 were tuberculous in origin. The fistulas in our case were secondary to a large staghorn calculus in the kidney pelvis with pyelonephritis.

The diagnosis is usually made by retrograde pyelography. In our case the ureteral orifice could not be located so the diagnosis was not established until examination of the specimen, although a renocolic fistula was suspected because of the changes seen on the barium enema. The formation of a renocolic fistula is often accompanied by severe pain complicating an episode of pyelonephritis, followed by passage of pus and blood from the colon, with cessation of the fever and flank tenderness. The fistula may be present for many years before definitive treatment is sought. The patient in the present report probably acquired his fistula 5 years previous to admission, coincident with the severe left costovertebral pain.

Ratliff and Barnes found an operative mortality of 33 per cent in the literature and advocated conservative methods of treatment. The usual surgical procedure has been nephrectomy with ligation or closure of the fistulous tract into the colon. Frequently a fecal fistula is formed in the wound due to reopening of the colon. Because of the poor results that have attended this method, we believe that surgical treatment should include resection of the involved segment of colon in addition to nephrectomy.

SUMMARY

A case report of spontaneous renocolic fistula has been presented with a brief review of the etiology, diagnosis and treatment.

The value of resection of the involved segment of colon has been emphasized.

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EXPERIMENTAL SUBSTITUTION OF THE COMMON BILE DUCT WITH AN AUTOLOGOUS URETERAL GRAFT

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Organ substitution has long been an interesting and difficult problem. Many important advances have been made, some of the most recent being substitution of isolated segments of large bowel for the stomach or urinary bladder and use of a portion of the stomach for esophagus.[1, 2] In the Roux Y procedure an antiperistaltic segment of jejunum is used as a substitute for the biliary ducts when they are irreparably damaged or strictured. This operation is fairly satisfactory but difficulty due to strictures may develop, postoperatively.

Experimentally, other attempts at substitution for the common bile duct have been made. Lord and Chenoweth[3] used free grafts of fascia, vein and peritoneum in dogs to substitute for sections of the common duct. Recently, Sedgwick reported the reconstruction of the common bile duct in three dogs with 2 to 3 cm. segments of ureter used as free grafts.[4] Creighton and Kittle have also recently reported their experience with free arterial and split thickness skin grafts in bridging defects in the common bile duct of the dog.[5] Large segments of ureter have never before been substituted for the common bile duct.

Pearce and Eisenbrey anastomosed the right renal pelvis to the common bile duct in order to exclude bile from the intestinal tract of dogs without an external fistula.[6] The right kidney was removed, bile then passing from the common duct down the right ureter and into the urinary bladder. Much difficulty was encountered due to leakage at the suture line and formation of strictures. Five dogs lived 49 to 248 days. The ureter tolerated the bile fairly well over a long period showing some epithelial atrophy, fibrotic thickening, lymphoid cell infiltration and either narrowing or dilatation of the lumen.

Kapsinow, Engle and Harvey performed cholecystnephrostomy in dogs for the same purpose as indicated above with the likelihood of stricture eliminated.[7] Bile

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passed from the gallbladder into the right kidney and down the right ureter to the urinary bladder. The kidneys apparently did not tolerate the bile and became atrophied shells. Again, the ureters seemed to tolerate the bile fairly well.

As it would appear that the ureter could tolerate the continuous passage of bile, for a limited time at least, it was decided to attempt substitution of a large segment of ureter with an intact blood supply for the common bile duct.

METHODS

The procedure was done in three stages. Medium-sized mongrel dogs were used. At the first stage the right ureter was doubly ligated and divided near the bladder. The ureter was then stripped proximally for a distance of from 10 cm. to as much as the entire length. This stage was concluded by placing the end of the ureter up near the kidney where it would be accessible at the second operation. The purpose of the first stage was twofold. By ligating the ureter it became dilated within a few days to a workable size, usually three times the normal diameter. Stripping the ureter towards the kidney stimulated the blood supply from the proximal end of the ureter, much as in a pedicle graft of skin.

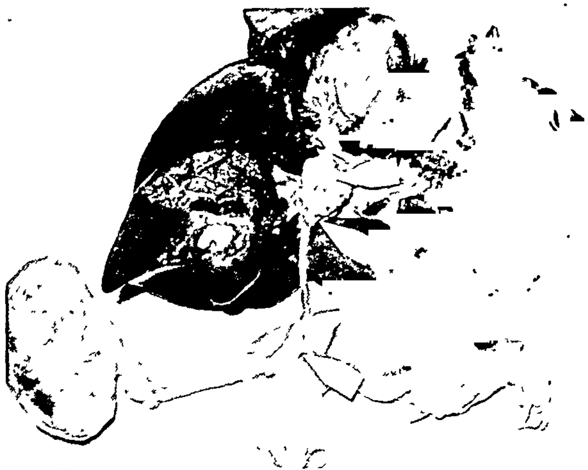

FIG. 1. Reconstructed biliary tract of dog 3. This was customary operative result prior to removal of excess ureter and kidney at third stage of procedure. Common bile duct has been replaced by distal one-half of ureter for 17 weeks. Lower arrow is directed toward side-to-side ureterojejunal anastomosis. Middle arrow is directed toward end-to-end anastomosis of distal end of ureter with proximal stump of resected common bile duct. Uppermost arrow points toward opened dilated common bile duct above ureterocholedochal anastomosis. Note the dilated gallbladder and hydronephrosis.

The second stage was done one week later through a high vertical abdominal incision. The dilated ureter was picked up and completely stripped to the renal pelvis if this had not previously been done. The common bile duct was then dissected free and divided near the duodenum after ligating the distal end. A T-tube was then inserted in the common duct through a small longitudinal incision about 2 cm. proximal to the free end. The distal arm of the tube projected 2 cm. beyond the end of the common duct in order to splint the ureterocholedochal anastomosis. After freshening the distal end of the ureter, it was swung upwards and anastomosed to the common duct, end-to-end, with interrupted 4-0 atraumatic chromic catgut sutures. A side-to-side, mucosa-to-mucosa anastomosis was then performed between the ureter and the proximal jejunum using the same suture technique. The length of ureter interposed between bile duct and jejunum varied from 8 to 10 cm. The wound was then closed and about two weeks later the T-tube was removed (fig. 1).

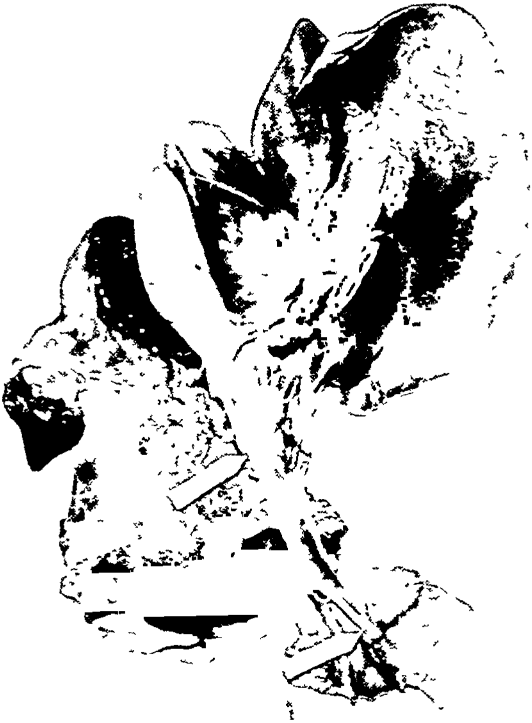

FIG. 2. Reconstructed biliary tract of dog 4. Distal one-half of right ureter has served as a substitute for common bile duct for 26 weeks. Right kidney and unused portion of ureter were removed in third stage of operative procedure. Lower arrow is directed toward wooden applicator projecting through ureterojejunal anastomosis. Upper arrow points toward ureterocholedochal anastomosis. Muscular tube between two arrows is segment of ureter which has been entirely separated from all normal anatomical connections. Bile ducts above uretero-choledochal anastomosis are moderately dilated.

At intervals varying from one to six months after the second stage, the right kidney and excess ureter were removed leaving a segment of ureter 8 to 10 cm. long serving as a substitute for the common bile duct (fig. 2).

RESULTS

Eleven dogs were operated upon with one operative death, presumably due to excess anesthesia. There was a delayed postoperative mortality of 5 dogs due to peritonitis caused by leaks at one or both anastomoses. Five dogs lived from 1 to

6 months. One of these died 4 weeks, postoperative, with peritonitis due to drainage of infected urine into the peritoneal cavity through a retracted nephrostomy tube. (A nephrostomy was done on this dog in an attempt to minimize kidney damage.) One dog died at 6 months having had the third stage performed 2 months previously. Autopsy revealed an atrophic liver with severe chronic cholangeitis and hepatitis. The three remaining dogs were sacrificed at 4, 5 and 6 months.

The necropsy findings in the latter three dogs were essentially identical. All anastomoses were patent with no evidence of stricture except for moderate narrowing of one ureterocholedochal anastomosis. There was slight to marked dilatation of the bile ducts above the ureterocholedochal anastomosis. (figs. 1 and 2). The bile was turbid and grossly infected, hair being found in the biliary ducts in two cases. With one exception the livers showed varying degrees of gross chronic infection of an ascending cholangeitic type. The ureteral grafts had not changed from their appearance at the second stage, retaining the dilatation and moderate muscular hypertrophy. The grafts were all viable with no evidence of atrophy, while the mucosa appeared everywhere intact and free from inflammatory changes.

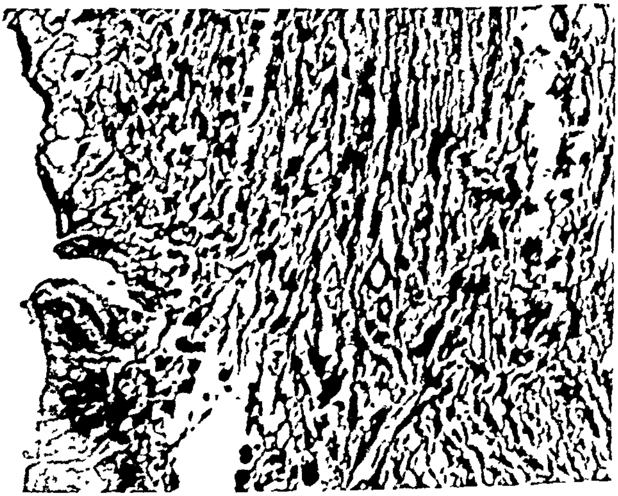

FIG. 3. High power photomicrograph shows a hea anastomotic junction. Intimate approximation of darkly stained ls of common bile duct with lightly stained layers of transitional ter is shown. Beneath both types of epithelium, layer of dense scar tissue is present, formed during healing of anastomosis.

DISCUSSION

By these experiments we have shown that a large segment of denervated ureter can be utilized as a substitute for another tubular organ and develop an entirely new blood supply. The utilization of the right ureter as a common bile duct is possible, but not practical, as done by the method outlined here. As in previous biliary tract surgery, the main difficulty, aside from technical ones, was regurgitation of intestinal contents up the bile ducts with subsequent infection of the liver. In our opinion, this regurgitation was due to the absence of a valve at the ureterojejunal anastomosis.

The technical difficulties consisted of inadequate operative exposure by the abdominal approach and leaks at one or both suture lines. We believe that with a combined thoracoabdominal approach and adequate surgical assistance the technical difficulties of this operation would be greatly decreased.

It would not be necessary to remove the right kidney to do this operation. Nephrostomy, ureterostomy or ureterocolostomy could be performed to assist in preservation of renal function.

Experimentally, the kidney was removed to prove that no normal anatomical connections of the transplanted ureteral segment were needed for its survival and retention of structure as a whole graft.

The retention of structure of the ureter in its transplanted location was of some practical and theoretical interest. It is to be remembered that the transplanted segment of ureter was separated from all normal anatomical connections. New blood supply was established by vascular penetration into the transplant at the two sites of anastomosis. The possibility of establishment of new neural connections was not investigated, but muscular atrophy did not occur so that it may be assumed that the smooth muscle remained active. The extent to which this activity might have assisted regurgitation from the jejunum or otherwise interfered with the normal flow of bile by uncoordinated peristaltic action is being investigated.

A matter of further interest was the persistence of transitional epithelium of the graft. Junctions of this epithelium to the epithelium of the common bile duct and the jejunum were closely established in anatomical continuity without the formation of strictures (fig. 3).

SUMMARY

An operation for replacement of the common bile duct of dogs with a large segment of the right ureter was described. In the first stage the lower end of the right ureter was ligated. The second stage, done a few days later, involved two anastomoses. One was between the distal end of the dilated ureter and the proximal stump of the resected common bile duct, the other was between the proximal right ureter and the jejunum. After allowing time for establishment of a collateral blood supply, the transplanted segment of ureter was separated from its normal anatomical connections. The transplant persisted as an epithelialized muscular tube which conducted bile satisfactorily. Although no strictures developed, the transplant failed to prevent regurgitation of jejunal contents and subsequent chronic cholangitis and hepatitis.

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FOREIGN BODIES IN URETER: A COMPLICATION FROM USE OF ELECTRODES FOR URETERAL MEATOTOMY

JAMES C. VALENTA AND CARLIN V. CHENOWETH

Foreign bodies of the ureter are rare. The literature lists and describes numerous and sundry objects which are found in the urethra and urinary bladder. In a survey of the literature over the past 25 years, it is noteworthy that the incidence of ureteral instruments which have been lost or impacted in the ureter by urologists in quest of ureteral stones is great. An impacted ureteral instrument, even though detached, is analogous to a foreign body. Heretofore, reports for the most part have indicted the numerous ingenious ureteral instruments, or their attachments, which have been designed for the removal of ureteral stones. We wish to report two interesting case histories, the ureteral instrumentation in which did not have as its aim the removal of impacted ureteral stones. In both instances, ureteral meatotomy electrodes with flexible filiform tips were the instruments which were used. The portions that became detached and impacted were the filiform tips.

The literature survey revealed that ureteral "foreign bodies" are rare. Rusche and Bacon list one incidence of a detached Howard spiral stone dislodger, in a series of 8,862 ureteral instrumentations at the Los Angeles County General Hospital subsequent to January 1, 1928. This was removed by ureterotomy with an uneventful recovery. W. Dakin described the loss of the threaded filiform tip of a ureteral stone basket. Fortunately, the operator was able to re-thread and retrieve the tip without incident. In 1943, W. N. Wishard reported an instance of an incarcerated, but intact Johnson stone basket. Endoscopic manipulation failed and the eventual treatment was ureterotomy. Klika removed a knotted ureteral catheter by incision of ureter and bladder with a "tenotome." Healing was complete in three weeks.

CASE REPORTS

These 2 cases emphasize the possibility of breaking and losing the filiform portion of ureteral meatotomy electrodes.

Case 1. C. C., a white woman, aged 68, entered St. Luke's Hospital September 10, 1951 because a metallic object had been discovered in the upper one-third of the right ureter on a barium enema x-ray film. These films were not available. She had undergone right ureteral meatotomy in April 1951 in another city.

Physical examination was essentially negative. All laboratory reports were essentially normal except for a microscopic hematuria.

An excretory urogram of September 10, 1951 revealed an essentially normal pyelogram except for the presence of a metallic object (fig. 1, *A*).

An abdominal scout film, which was taken just before surgery on September 13, 1951 localized the "foreign body" in the lower one-third of the right ureter

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This material is presented from the urological services of T. P. Grauer, M.D. and W. J. Baker, M.D., St. Luke's Hospital, Chicago, Ill.

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(fig. 1, *B*). So an ureterotomy was done through a Gibson incision. A careful exploration of the ureter failed to disclose the object. Another abdominal scout film was done on the operating table and it revealed that the instrument had ascended to the ureteropelvic junction (fig. 1, *C*). The muscle and skin incisions were extended, and the instrument was "milked" downward to the original ureterostomy, through which it was removed. The object was identified as a Bard U.S.C.L. No. 4. filiform tip which had been attached to the distal threaded portion of a Bard 617 ureteral meatotomy electrode (fig. 2).

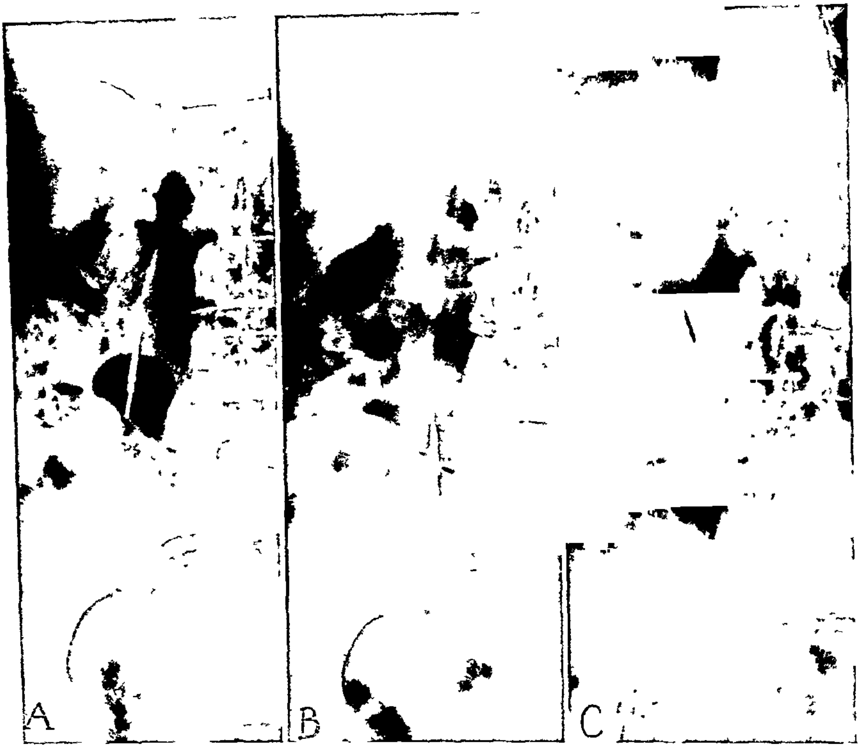

FIG. 1. Case 1. *A*, excretory urogram showing filiform tip of ureteral meatotomy electrode in right ureter. *B*, preoperative film showing presence of filiform tip of ureteral meatotomy electrode. C, film taken on operating table showing tip of ureteral meatotomy electrode had ascended to ureteropelvic junction of right ureter.

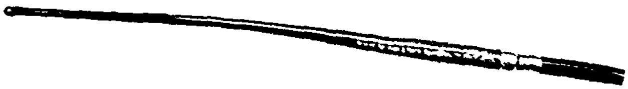

FIG. 2 Case 1 Bard No. 4 filiform tip on broken end of Bard No. 617 ureteral meatotomy electrode

The patient made an uneventful recovery.

Case 2. A. R., a female, aged 56 years, was admitted to St. Luke's Hospital, July 2, 1951 for treatment of a "foreign body" in the left ureter. The patient had had a cystoscopic left meatotomy for a left ureterocoele.

Physical examination was essentially normal. Laboratory findings were well within normal limits except that cultures of the urine revealed two colonies of Staphylococcus aureus and some diphtheroids.

Excretory urography revealed a normal right kidney and a double renal pelvis and ureter on the left side (fig. 3, *A*). The ureteral instrument was situated in the lower portion of the middle one-third of one of the left ureters.

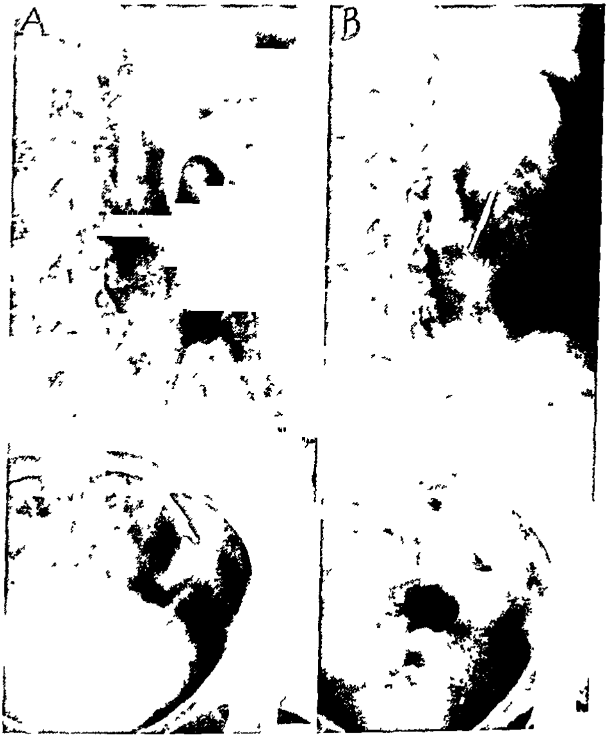

FIG. 3. Case 2. *A*, excretory urogram showing filiform tip of meatotomy bougie in lower third of left ureter. *B*, film taken on operating table showing filiform tip of meatotomy bougie had ascended to upper third of left ureter.

It was believed that a period of "watchful expectancy" was indicated with the hope that the filiform would pass spontaneously. This hope was not realized and therefore, on July 9, 1951 an attempt to retreive the filiform by cystoscopic means was made. This was unsuccessful.

An x-ray film taken July 11, 1951 on the operating table localized the object (fig. 3, *B*). Under spinal anesthesia, a ureterotomy was performed and the filiform tip with a portion of the working element was removed. The object was identified as a portion of a Bard No. 8 meatotomy bougie.

The patient experienced an uneventful convalescence and was discharged July 20, 1951.

An attempt was made to determine the maximum current which would cause a new bougie to undergo structural breakdown. A piece of meat measuring 1 by 3 by 2 inches was immersed in a pan of water. A groove was made with a probe and the bougie was inserted. The Bovie unit was then set at increasing cutting currents starting at 10 and ending at 100. After one trial at each successive increase in current, the meatotomy bougie was intact. Thus, in this one case, current did not seem to be a factor in the structural breakdown.

CONCLUSIONS

Ureteral "foreign bodies" are rare and of these cases heretofore reported, the ureteral instruments designed for the removal of impacted ureteral stones were the main offenders.

Two cases of broken and impacted filiform portions of ureteral meatotomy electrodes have been reported. These meatotomy bougies are potentially dangerous instruments. The eventual treatment of both patients was ureterotomy and removal of the filiforms. The patients made uneventful recoveries.

An attempt was made to determine whether the strength of the cutting current was a factor in the structural breakdown of meatotomy bougies. This did not seem to be a factor.

St. Luke's Hospital, Chicago, Ill.

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THE USE OF CORTISONE IN INTERSTITIAL CYSTITIS: A PRELIMINARY REPORT

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Interstitial cystitis is a disease whose etiology is unknown, whose symptoms are severe and often incapacitating, and whose treatment is palliative. Endoscopic fulguration of the lesions plus hydraulic dilatation of the bladder repeated at sufficiently frequent intervals to maintain bladder capacity have produced the best symptomatic results in my experience. Even here, however, improvement is usually temporary and there is less favorable response to each succeeding fulguration. Eradication of foci of infection and the instillation of gradually increasing concentrations of silver nitrate into the bladder have been followed with disappointing results in my hands. I have had no experience with partial cystectomy, endoscopic division of the fibrous trabeculae, direct injection into the bladder wall of novocaine, oral alpha-tocopherol, or radiation in treating this disease.

Since there is at present no ideal palliative or curative treatment for interstitial cystitis, it seemed worthwhile to explore the possibilities of a different approach to the management of this distressing and incapacitating condition. When the beneficial effect of adrenocorticotrophic hormone (ACTH) and cortisone on certain collagen diseases was first described, it seemed possible that these drugs might favorably influence the course of interstitial cystitis which, in some respects, is similar to the recognized collagen diseases.

I wish to report at this time my experience with the use of cortisone in the treatment of interstitial cystitis and would like to make it clear at the beginning that my findings do not indicate that cortisone cures this disease. However, I believe that it can be demonstrated that systemic administration of cortisone alone, with no other treatment whatsoever, so favorably affects the symptoms and bladder capacity of some of these individuals with interstitial cystitis that, even though the maximum improvement is temporary, it dramatically alters their clinical condition.

Shortly before my first patient was treated in this manner, Dr. Victor Marshall[1] told me of three patients who had been treated by Paquin and himself with ACTH who showed temporary improvement while receiving medication but relapsed when medication was discontinued. Weaver and Tyler[2] describe similar results and observations in a group of 4 cases. Sullivan[3] has recently reported rather prolonged improvement in 2 patients treated with a single week's course of cortisone.

Merck and Co. generously supplied the cortisone used in this investigation.
Read at annual meeting, American Urological Association, Atlantic City, N. J., June 25, 1952.

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The effect of the 2 drugs is thought by most observers to be identical. The response to administration of the pituitary hormone, ACTH, depends upon the ability of the adrenal to respond to stimulation by an increased output of cortisone, thus the clinical effect may disappear during continued administration if adrenal exhaustion occurs. Cortisone on the other hand directly increases the blood level of the circulating steroids. Among many metabolic effects produced by the two drugs, those that are most pertinent to the present discussion include depression of the total eosinophil count, increase in blood sugar, and varying degrees of hypertension. Excretion of potassium, chloride, calcium and phosphorus is increased, whereas sodium is retained in the body thus tending to cause edema. The local antigen-antibody reaction is inhibited which may lead to aggravation of tubercular and other infections. Inflammatory reaction is decreased.

These drugs are contra-indicated in cases of peptic ulcer, active tuberculosis and other active infections that cannot be well controlled by specific antibiotics. Relative contra-indications, or at least the need for very cautious administration, exist in the presence of diabetes, hypertension, congestive heart failure, and certain psychiatric disorders.

The patients selected for treatment with cortisone have had long standing, severe symptoms of interstitial cystitis which were not controlled adequately by fulguration and hydraulic dilatation of the bladder. In all patients, determination of the body weight, blood pressure, blood calcium, phosphorus, chloride, potassium, CO_2 combining power, and total eosinophil counts were obtained prior to treatment. Determinations of the blood pressure, weight, total eosinophil count and glycosuria were obtained daily during the first 2 weeks of treatment and at less frequent intervals thereafter. For varying periods prior to treatment and during the first 2 weeks of cortisone therapy an accurate record was kept of the volumes of each individual voiding day and night. The patients were instructed to hold the urine as long as possible before voiding. Following discharge from the hospital throughout the period of cortisone administration, and at periodic intervals thereafter, accurate records of the volume of each voiding between 7 p.m. and 7 a.m. were obtained. The average, the average minimum and the average maximum volume of the patients' individual voidings were computed on a weekly basis as follows: For the average volume voided, the volumes of each individual voiding for the 24 or 12 hour period were added and divided by the number of voidings. This figure was obtained for each day of the 7 day period, the 7 figures then being added and divided by 7 to give the average volume of individual urinations per week. For the average minimum voiding, the two smallest voidings in each 24 or 12 hour period were averaged and the 7 figures thus obtained for a weeks period were added and divided by 7. The average maximum voidings were determined in a similar way. Except for the first course of treatment in the first patient treated, cortisone has been administered by mouth. The schedule of dosage has varied to some extent, however, most patients received 300 mg. the 1st 24 hours, 200 mg. the second 24 hours and 100 mg. daily for a total of 2–3 weeks. The dosage was then reduced to 50 mg. daily for periods varying from an additional 2 to 6 weeks or longer. The daily dose was administered in 4 equal parts at 6 hour intervals. Recently, they have received a low salt diet and potassium ABC (acetate, bicarbonate and citrate) 3 gm. t.i.d. during administration of cortisone.

All of the patients in this group treated with cortisone had moderate to severe typical suprapubic pain when their bladders became distended. They showed no evidence of active tuberculosis, had normal upper urinary tracts as shown by abdominal x-ray and excretory urography, and had normal urinalyses except for the presence of a few red blood cells unless otherwise stated. In all cases there was a decrease in the total eosinophil count during the first few weeks of therapy to 50 per cent, or less, of the pretreatment level which is accepted as indicating adequate response to cortisone administration.

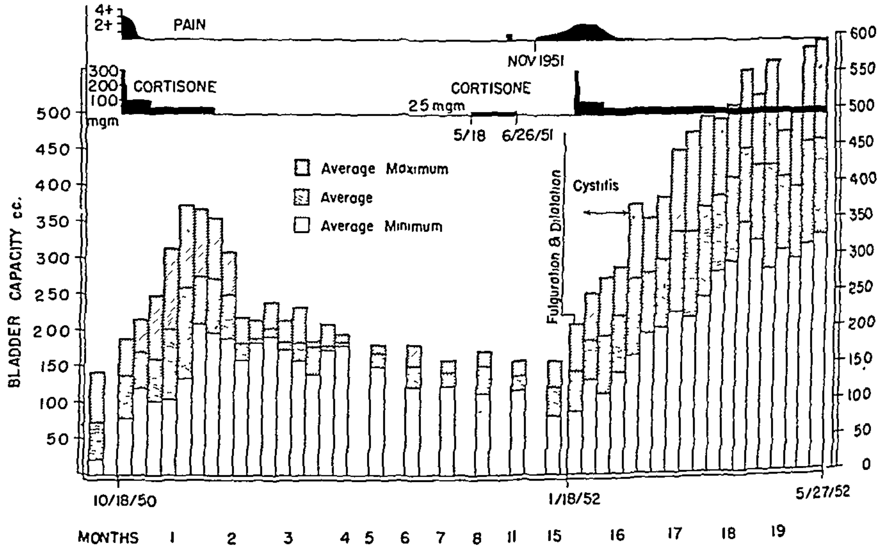

Fig. 1

CASE REPORTS

Case 1. Mrs. J. P., a 55 year old woman, was first seen in March 1949, with a complaint of urinary frequency and suprapubic pain for more than 3 years, it being necessary for her to void at least once an hour both day and night. Typical interstitial cystitis was discovered and treated by fulguration and dilatation of the bladder with considerable improvement for the following 8 months. Her symptoms recurred and treatment was repeated in April 1950, with negligible improvement and she continued to void every 1 to 1½ hours, having marked pain with a full bladder. On September 19, 1950, cystostopy showed three areas of typical interstitial cystitis. One month later, on October 18, the patient was admitted to the hospital with her symptoms unchanged. Twenty-four hours after admission, a course of cortisone therapy was instituted, treatment being discontinued December 1, 1950. During this time she received no other treatment or instrumentation whatsoever. Cystoscopy carried out 2 weeks after her last dose of cortisone showed only one small area of interstitial cystitis measuring 2 by 3 mm. in diameter just to the right of the air bubble, the other two areas having disappeared. Her suprapubic pain disappeared completely before the end of the first week of cortisone therapy.

As will be seen from figure 1, the patient's average maximum voidings increased from a pretreatment level of 142 cc to approximately 270 cc during the last 2 weeks of her first course of cortisone. The average minimum voidings increased from a pretreatment level of 20 cc to 210 cc during the last week of treatment. There was then a gradual decrease in capacity so that 10 months after treatment had been stopped, voidings were ranging between 120 and 170 cc. Even then, however, she was arising only twice at night to void and during this entire year had no vesical pain. During the thirteenth month, there was re-appearance of the suprapubic pain which slowly increased to become moderately severe.

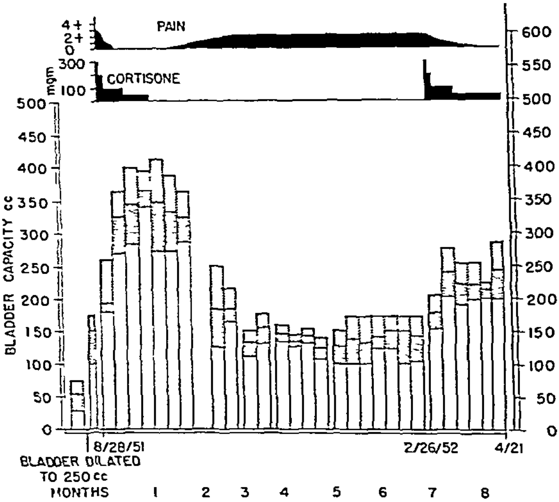

FIG. 2

Fifteen months after initiation of treatment the patient was admitted for further therapy. Cortisone was again administered and 3 days later under anesthesia, 3 areas of interstitial cystitis were fulgurated and the bladder hydraulically dilated to 400 cc. Her pain disappeared somewhat slowly but finally was negligible 4 weeks after starting her second course of cortisone. The bladder capacity progressively increased so that by the nineteenth week of treatment, her average voidings were approximately 450 cc and the average maximum and minimum voidings were 600 cc and 325 cc respectively.

Case 2. G. E. H., a 34 year old white married woman, was admitted on August 24, 1951 giving a history of urinary frequency and suprapubic pain for the preceding 3 years. Nocturia was 10 to 12 times at the time of admission. Voidings during the first few days of admission varied from 30 to 75 cc in amount. Cystoscopy on the third day of hospitalization revealed numerous confluent areas of interstitial cystitis occupying the dome and lateral walls of the bladder whose capacity was 90 cc. The bladder was inadvertently dilated to 150 cc during cystoscopy and for the following 2 days her voidings were slightly greater in amount, ranging from 100 cc to 175 cc (fig. 2).

On August 28, 1951, cortisone therapy was commenced. Four days after commencing cortisone, her severe suprapubic discomfort had completely disappeared and her individual voidings were averaging 250 cc. Maximum improvement occurred at the end of the course of cortisone at which time her average minimum and maximum voidings were ranging between 275 and 412 cc. One week after the last dose of cortisone there was a gradual recurrence of her pain and a progressive decrease in the bladder capacity. Between the third and seventh month after institution of treatment, her symptoms apparently stabilized with minimum and maximum voidings ranging between 100 and 175 cc. Her pain persisted to a moderate degree. Even with this decrease in bladder capacity however, she was still awakened only twice a night to void as contrasted to a nocturia of 10 to 12 times prior to treatment.

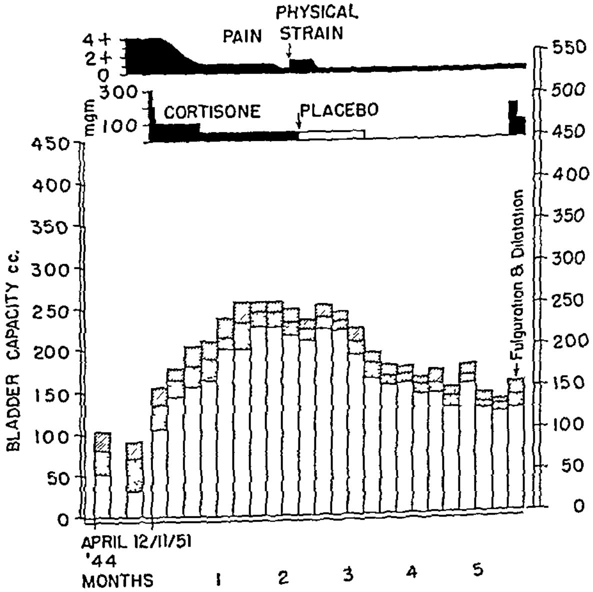

FIG. 3

Seven months after institution of treatment, she was started on a second course of cortisone by her local physician at our direction but not under our personal supervision. Her biweekly reports of her symptoms and individual voidings indicate that her pain is again subsiding and her bladder capacity increasing under cortisone therapy, though not as dramatically as with the first course of treatment.

Case 3. F. T., a 53 year old man, was first seen in April 1944, at which time he had had marked urinary frequency and suprapubic pain since 1929. There was nocturia of 10–12 times and his pain was extremely severe. Under anesthesia three areas of interstitial cystitis were fulgurated and the bladder was dilated to 200 cc. For the following 5 months the patient was treated frequently with hydraulic dilatations of the bladder and instillations of silver nitrate with absolutely no improvement in his symptoms or bladder capacity. His voidings ranged from 75 to 100 cc each, and his severe pain persisted unabated.

The patient then disappeared from observation, received no treatment, and his symptoms remained unchanged until he was again seen in September 1951. At that time he was having excruciating suprapubic pain whenever his bladder became full. During the 4 days prior to his admission the average minimum and maximum voidings were 30 and 90 cc respectively (fig. 3). Cystoscopy on December 10, 1951 revealed a bladder capacity of 90 cc. There was one area of interstitial cystitis near the air bubble on the anterior bladder wall and another large area of diffuse involvement of the right side of the bladder wall extending down to the bladder neck. Cortisone was commenced on December 11, 1951. Approximately 7 to 10 days after institution of cortisone therapy the patient's pain gradually became better so that even though some discomfort was experienced when his bladder was quite full, it was practically negligible. The greatest improvement in bladder capacity occurred during the last 4 weeks of cortisone therapy and the first 3 weeks that he received a placebo. During this time his average minimum and maximum voidings varied from approximately 220 cc to 260 cc. Thirteen weeks after stopping cortisone, his pain was still negligible and nocturia amounted to only 1 or 2 times for the first time in 23 years although his bladder capacity had decreased to range between 120 and 140 cc. Recently, a second course of cortisone was started and, on the fourth day the bladder was dilated to 300 cc under anesthesia and 2 small areas of interstitial cystitis were fulgurated. From the standpoint of symptomatic improvement, this patient was the most impressive in the group because of the extreme severity and long duration of his symptoms.

Three additional cases have been treated and followed for shorter periods of time than those just reported. In two, improvement has been much less spectacular, but an excellent immediate response has occurred in the third.

DISCUSSION

In so far as I am aware, cortisone does not cure any of the diseases in whose treatment it has been shown to be of such great value. In status asthmaticus it produces dramatic disappearance of the explosive features of the attack but does not cure the underlying cause of the allergy nor does it prevent subsequent attacks. In rheumatoid arthritis the acute inflammation of the involved joints and the severe pain attendant thereon rapidly disappear, but there is usually a recrudescence of the arthritis after discontinuing cortisone unless a natural remission of the disease occurs. As the course of interstitial cystitis usually is not marked by natural remissions as are diseases like rheumatoid arthritis, rheumatic fever and asthma, it seems only natural to expect a recurrence of symptoms after discontinuing therapy. In case 1, it is interesting to note that vesical pain disappeared under treatment and did not recur until thirteen months later. Although the bladder capacity progressively decreased after cortisone was stopped, the minimum voidings remained much larger than prior to therapy and at the end of a year, although the bladder capacity was varying between 120 and 150 cc, the patient found it necessary to rise only twice at night to void. Case 2 showed similar prolonged improvement in urinary frequency although there was rapid reappearance of moderate vesical pain. Case 3, although exhibiting less dramatic improvement in actual bladder capacity than patients Nos. 1 and 2, has had the most spectacular relief of his bladder symptoms of any patient in this group. This has transformed him from a person completely incapacitated for more than 23 years to a man who now can carry on practically normal activities.

I believe that there is no question but that cortisone increases bladder capacity and decreases or abolishes vesical pain in some cases of interstitial cystitis and that it may well have a definite place in the treatment of this disease. Whether it should be used in conjunction with local treatment, administered in a prolonged course extending over many months, in frequent short interrupted courses, or in some other way can only be determined after further experience with the drug in treating this disease has been accumulated. The results in cases 1 and 2 in this series suggest that the combination of physical and hormonal treatment is desirable. This is in line with observations on the management of patients with chronic allergies and chronic rheumatic arthritis.

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URETEROSTOMY-IN-SITU

SAMUEL N. VOSE AND GRANT M. DIXEY

The problem of diversion of the urine from the bladder is interesting and often troublesome. At present in radical surgery for carcinoma of the bladder, uretero-enterostomy is recognized as a satisfactory method in most instances. However, there are cases in which progressive obstruction, with consequent infection or diminution of renal function, occurs and it becomes necessary to utilize another type of drainage. For this purpose the following procedures have been used; namely, cutaneous ureterostomy, nephrostomy and pyelostomy.

Nephrostomy over the years has proven to be a fairly efficient method of diversion of urine. In patients with large extrarenal pelves, drainage is usually satisfactory and tube change is not too difficult. The patient with smaller intrarenal pelves presents more problems since the procedure is technically more difficult and subsequent catheter changes may be of major surgical proportions. The location of the tube in the flank or the back is a serious disadvantage. Furthermore, the insult to renal tissue due to the trauma of the original procedure and subsequent tube changes may result in renal deterioration and progressive insufficiency.

Pyelostomy as a type of permanent diversion is rarely used.

Ureterocutaneous anastomosis has received considerable attention in the literature and the various techniques described for this operation testify to the somewhat unsatisfactory status of the procedure as a whole. The authors' experience with this method has been limited but mostly unsatisfactory. Strictures are not uncommon and subsequent peri-ureteral abscess formation is a frequent complication. Huggins, in discussing cutaneous ureterostomy, states that an inlying catheter should be used, and that strictures occur not at the ureteral ostium but several centimeters beneath the skin.

A brief consideration of the normal anatomy and physiology of the ureter, with its course through loose areolar tissue, demonstrates why displacement of this structure to traverse muscle and fascia with co-incident interference with blood and nerve supply may result in stricture formation.

Recently we have re-employed a method of secondary diversion which involves no displacement of the ureter and which has functioned satisfactorily in a small series of cases. Briefly, it establishes a permanent or semi-permanent fistula between the ureter and the skin by a simple intubated ureterostomy, an operation which all of you have performed many times and which needs no detailed description. This fistula lined by granulation tissue tolerates a catheter much better than the epithelial lining of the ureter and changing of the catheter has proved extremely easy. The ureter is approached by the customary route for operation on the middle third. Without disturbing the normal course and relation of the ureter an incision is made in the wall, the tip of a catheter inserted

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Read at annual meeting, American Urological Association, Atlantic City, N. J., June 24, 1952.

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and advanced upward to the renal pelvis. The other end of the catheter is exteriorized through the lower angle of the incision, which is closed in customary fashion.

The first case in which this method was used illustrates the procedure and course. In 1939, at age 58, a transurethral prostatectomy was performed, and urologically the patient was well until October 1949, at which time after a bowel resection for carcinoma he had postoperative urinary retention, necessitating constant drainage. In March 1950, because of persistent urinary infection, he was seen by us. Cystoscopy revealed marked trabeculation, cellule formation and chronic inflammatory changes. The bladder neck was unobstructed but there was some intrusion of the left lateral lobe of the prostate into the posterior urethra. The urinary infection was treated by means of the usual urinary antibacterial agents with control of infection while the drugs were administered but recurrence took place promptly after cessation of their use. In June 1950, a transurethral resection of the residual prostatic tissue was performed with biopsy of a suspicious area on the floor of the bladder. Pathologically these tissues revealed only inflammatory changes.

Because of the persistence of distressing symptoms, he was re-admitted to the hospital in October 1950, and a suprapubic cystostomy done. Biopsy of an area in the region of the trigone proved to be infiltrating carcinoma. Consequently, on November 10, 1950, a total cystectomy and bilateral ureterosigmoidostomy was done. In the next 4 days there was no urinary output and the nonprotein nitrogen rose to about 140 mg. per cent. The patient was becoming critically ill and some form of drainage was imperative. Excretory urography prior to cystectomy had shown very poor function in the right kidney and it seemed that left ureterostomy would provide the maximum benefit with the least formidable operative procedure in the case of this extremely sick patient. The ureter was approached through a low flank incision, as is customarily used for operations on the middle third of the ureter. The dilated ureter was identified, a longitudinal incision in its wall made, without disturbing the ureteral course and a No. 20 Foley catheter passed up to the renal pelvis. The 5 cc bag was inflated and the wound closed. From then on, the patient's recovery was rapid, and he was discharged on December 18, 1950.

It was our intent to allow the patient to convalesce prior to further definitive surgery, either nephrostomy or cutaneous ureterostomy, which we feared would be necessary as we had grave misgivings about replacing the tube should it become occluded. Our fears were soon realized for on December 26 the patient came to the office complaining that the tube was not draining. Attempts to free the obstruction in the catheter were unsuccessful and it was removed. Much to our delight there was no difficulty in inserting another Foley catheter. The following day the patient returned with the information that during the night the bag on the Foley had broken and the catheter fell out. Not wishing to disturb anyone he waited until morning before seeking help. Again a catheter was inserted without difficulty. Subsequent changes of the catheter were carried out at intervals of 2 to 6 weeks without difficulty, in several instances by the patient's son, who is a pharmacist.

Case 2 is a 44 year old man who had transurethral resection of a bladder tumor which revealed undifferentiated carcinoma of bladder. In May 1949, a total cystectomy, lymphadenectomy and bilateral uretero-enterostomy was done. Excretory urograms revealed progressive hydronephrosis with diminution of function on the right side. There was mild hydronephrosis on the left but apparent good function. The nonprotein nitrogen rose slowly but steadily to 66 mg. per cent, and on July 15, 1950, a left nephrostomy was done. Nephrostomy drainage seemed adequate but the nonprotein nitrogen remained between 45 and 50. The nephrostomy tube was changed once without difficulty. In March 1951, the nephrostomy tube was draining poorly. The tube was removed and attempted replacement was unsuccessful; consequently, a left ureterostomy was performed. Recovery was prompt and the patient was discharged on the eighth day. The catheter has been changed at intervals of 6 weeks and there has been no technical difficulty. The nonprotein nitrogen has ranged from 25 to 33 mg. per cent. The patient, who is an extremely active lawyer, has been much more comfortable and content with his present arrangement than at any time since his original operation.

Case 3 is that of a 65 year old man, who was first seen in June 1947, because of a mass in his right flank, lymphedema of right leg and a nonfunctioning right kidney which was demonstrated by excretory urography. Examination revealed a hard, nodular enlargement of the prostate. Repeated attempts to catheterize the right ureter were unsuccessful. Estrogen therapy was started with prompt disappearance of the swelling of the legs and the mass in the right flank. He was kept on estrogens by his physician and was not seen by us again until July 1951, at which time excretory urograms revealed some obstruction at the lower end of the left ureter with moderate hydronephrosis. The nonprotein nitrogen was elevated to 60. Orchiectomy was done with the hope that carcinomatous involvement of the subtrigonal area might subside. But the nonprotein nitrogen rose progressively to 80 mg. per cent and a left ureterostomy-in-situ was performed on August 3, 1951. Since then the tube has been changed without difficulty and the nonprotein nitrogen on January 23, 1952 was 46. This patient has since died of cancer of the prostate, the ureterostomy functioning satisfactorily until his death.

The procedure has been used in several other cases which will not be reported in detail.

In most of our cases this operation has been done as a secondary procedure where obstruction has occurred and the ureter has become dilated. In this group we have used, for the most part, a No. 18 or 20 Foley catheter with a 5 cc bag. In 2 cases done at the Veterans Administration Hospital at West Roxbury at our suggestion a polyethylene straight tube has been used. In 1 case such a tube remained in place nearly 9 months without changing and was easily replaced after removal for inspection. Such a tube may be secured in place by a polyethylene disc cemented on at the proper level and fastened to the skin by adhesive.

In only one case have we chosen this procedure as a primary method of diversion of the urine through a normal ureter. In this patient one kidney was re-

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In only one case have we chosen this procedure as a primary method of diversion of the urine through a normal ureter. In this patient one kidney was removed because of calculus pyonephrosis, cystectomy was performed for carcinoma of the base of the bladder and the urine from the remaining kidney diverted by means of ureterostomy-in-situ. A No. 12 catheter was the largest which could be passed up to the kidney pelvis. This is a recent case and the tube has not yet needed change. So far drainage has been satisfactory and renal function adequate.

This procedure has proved to have several advantages over nephrostomy or ureterocutaneous anastomosis, as follows:

The surgery necessary to establish such drainage is minimal, involves no insult to renal tissue, can be performed on very ill subjects and requires no particular length of ureter to function satisfactorily. The incision in the ureter can be made as high as necessary.

The point of exit of the tube can be located in a convenient place, a distinct advantage over nephrostomy although not so in the case of cutaneous ureterostomy.

The tube is tolerated well and no strictures have developed. Tube change has been carried out without difficulty in every instance as an office procedure without anesthesia.

In common with nephrostomy this method is not necessarily permanent. In 1 case the tube was removed after improvement occurred in the original obstruction and the fistula closed within 24 hours.

In conclusion, it has been our experience that ureterostomy-in-situ has distinct advantages over more commonly used methods of secondary diversion of the urine. Although more extensive use of this procedure may demonstrate unsuspected disadvantages, to date they have not appeared.

From a recent conversation with another urologist, it seems apparent that we did not sufficiently emphasize the importance of having the catheter emerge from the ureter and the operative wound as nearly as possible in a straight line. Angulation at the point of entering the ureter may interfere with easy replacement of the tube following accidental or intentional removal.

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BLADDER CARCINOMA: 5 YEAR SURVIVAL

MAJOR FERRIS E. COOK, JR., USAF (MC) AND COL. J. C. KIMBROUGH, USA (MC)

From the Urology Section, Surgical Service, Walter Reed Army Hospital, Washington, D. C.

A study of bladder carcinomas treated at Walter Reed Army Hospital prior to 1946 has been carried out for the purpose of determining the efficacy of various surgical procedures used during that period. Surgical treatment was performed by several urologists. Sufficient clinical data and follow-ups were available in 54 cases. The pathological diagnoses are those from the Pathological Department of this hospital and were reviewed by the Armed Forces Institute of Pathology. The term "recurrence" in this paper means the appearance of a tumor anywhere in the bladder after the primary lesion has been removed.

VITAL STATISTICS

This series consisted of 45 males and 9 females. Only two of the patients were Negroes. The average age was 48 years, 29 of the patients being under 50 years and 25 over 50 years. The youngest patient was 22 years and the oldest 74. The average duration of symptoms prior to cystoscopy was 9 months. The presenting symptom of hematuria occurred in 40 patients, dysuria in 11, eneuresis in one, albuminuria in one, and nocturia in one. Routine urine cultures were positive in 31 patients. Unilateral hydronephrosis was present in 7 patients and bilateral in 4. There were 4 patients with hydronephrosis who survived 5 years. Autopsies were performed on 20 of the 21 patients who died. Bladder carcinoma with the associated obstructive renal pathology was present in 18 patients. There were two postoperative deaths, the first occurring from pneumonia on the nineteenth postoperative day, and the second from pulmonary embolus with infraction on the first postoperative day.

PATHOLOGICAL CLASSIFICATION

For the purpose of classifying the pathological diagnoses, the system of Jewett[1, 2] has been followed. Since surgical treatment was primarily by transurethral electroresection and suprapubic electroresection, the actual depth of infiltration could not be determined. Therefore the tumors have been classified only as noninfiltrative and infiltrative. Patients with noninfiltrative bladder carcinomas had a 62 per cent better chance of surviving 5 years than those with infiltrative lesions.

Patients with well differentiated papillary carcinomas (grade 1) had a 100 per cent 5 year survival. Those patients with slightly differentiated papillary carcinomas (grade 3) had a 17 per cent 5 year survival. Prognosis was poorest in

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[1] Jewett, H. J. and Lewis, E. L.: Infiltrating carcinoma of the bladder: curability by total cystectomy. J. Urol., 60: 107, 1948.

[2] Jewett, H. J.: Carcinoma of the bladder: influence of infiltration on the 5 year results following complete extirpation of the primary growth. J. Urol., 67: 672, 1952.

patients having undifferentiated carcinoma. If the papillary carcinomas are subdivided into single and multiple tumors, those patients with multiple tumors have the best prognosis.

Table 1

PATHOLOGY	LIVING 5 YEARS	DEAD WITH TUMOR OR LIVING WITH TUMOR
Noninfiltrative	31 (88%)	4 (12%)
Infiltrative	5 (26%)	14 (74%)
Well Differentiated Papillary	24 (100%)	0
Moderately Differentiated Papillary	10 (71%)	4 (29%)
Slightly Differentiated Papillary	1 (17%)	5 (83%)
Moderately Differentiated Epidermoid	0	1 (100%)
Slightly Differentiated Epidermoid	0	2 (100%)
Undifferentiated	1 (14%)	6 (86%)

Table 2

PATHOLOGY	TOTAL NO CASES	LIVING 5 YEARS	PER CENT LIVING 5 YEARS
Papillary Carcinomas			
Single	28	21	75%
Multiple	16	14	87%

Table 3

TREATMENT	NO	CURATIVE TREATMENT	RECURRENCES WITH CURATIVE TREATMENT	PER CENT RECURRENCES	NONINFILTRATIVE	INFILTRATIVE	LIVING 5 YEARS	PERCENT LIVING 5 YEARS
Transurethral Electroresection	31	26	12	46%	25	6	23	88%
Suprapubic Electroresection	13	10	3	30%	8	5	10	100%
Segmental Resection	7	5	2	40%	2	5	2	40%
Uretero-intestinal Anastomosis with Cystectomy	1	0	—	—	1	0	0	—
Uretero-intestinal Anastomosis without Cystectomy	1	0	—	—	0	1	0	—
Ureterocutaneous Anastomosis	1	1	0	0%	0	1	1	100%

SURGICAL TREATMENT

The types of surgical treatment of bladder carcinoma have been divided into six groups. The last three groups do not contain sufficient cases for evaluation. Treatment is both curative and palliative, and combined or not combined with radiation. Recurrences following transurethral resection were 16 per cent more common than after suprapubic electroresection although the actual percentage of infiltrative lesions was greatest in the second group. If patients treated palliatively are not considered, the 5 year survival in those treated by suprapubic electroresection is 100 per cent as compared to 88 per cent in the group treated by transurethral electroresection.

DISCUSSION

Admittedly this series of cases is few in number, but certain impressions can be gained as far as future surgical treatment of bladder carcinomas is concerned.

1) Early diagnosis, adequate treatment, and continued follow-up cystoscopic examinations every three months will increase the percentage of 5 year survivals of patients with carcinoma of the bladder.

2) The presence of hydronephrosis, either unilateral or bilateral, is a poor prognostic sign.

3) The pathological diagnosis of infiltration, regardless of the pathological grade, carries a much poorer prognosis than noninfiltrative tumors.

4) Multiple tumors had a greater percentage of 5 year survivals than single tumors. There are two reasons for this. There is a greater tendency to treat them by the suprapubic route; and when these tumors recur they are usually of the same pathological grade as the primary lesions.

5) Recurrences of carcinoma occur as a result of a multicentric origin in the bladder, inadequate resection, and implantation of tumor cells. All three can be combated by methods at our disposal, the first by intracavitary radiation, the second by complete resection of the tumor as determined by the pathologists, and the third by decreasing the amount of trauma in removal of the tumor by getting adequate exposure. Removal of carcinoma in multiple fragments violates the most fundamental principle of cancer surgery. Quantitative cancer cytology of bladder fluid preoperatively, during resection, and postoperatively would be valuable in evaluating the various surgical procedures. Tumor recurrences following transurethral electroresection should occur at the site of greatest trauma, namely, the bladder neck. This has occurred in 3 patients with grade 1 papillary carcinoma treated in the past year.

The treatment of bladder carcinoma at Walter Reed Army Hospital is as follows:

1) Transurethral electroresection and fulguration is indicated in small grade 1 and 2 noninfiltrating carcinomas. It is used as palliative treatment in the elderly, poor risk patient.

2) Suprapubic electroresection or excision is indicated in carcinomas greater than 1.5 cm. in diameter which do not infiltrate muscle.

3) Segmental resection of the bladder is indicated in carcinomas not involving the trigone or ureters, but which have invaded bladder muscle without extension outside the confines of the bladder.

4) If a recurrence takes place after any of the above methods of treatment, the patient should again be treated using the above criteria, and in addition should receive intracavitary irradiation to a dose of 8000 roentgens to destroy tumor implants and precancerous lesions of the bladder as described by Melicow.[3]

[3] Melicow, M. M.: Histologic study of vesical urothelium. J. Urol., 68: 261, 1952.

5) Cystectomy with uretero-intestinal anastomosis is indicated in carcinomas not amenable to segmental resection, and is the surgical procedure of choice in repeated recurrences. Radical lymph node dissection, although not a part of the procedure in the past, may be a curative procedure in some patients.

6) External radiation, cutaneous ureterostomy, and uretero-intestinal anastomosis without cystectomy, are indicated as palliative procedures.[4, 5, 6]

SUMMARY

Fifty-four cases of bladder carcinoma treated prior to 1946 have been reviewed. The presence of hydronephrosis and the pathological diagnosis of infiltration offer a poorer prognosis. Multiple tumors have a better prognosis than single tumors. The recurrence of carcinoma following surgical treatment has been discussed and a plan of treatment presented.

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[5] Dean, A. L., Mostofi, F. K., and Thomsen, R. V.: A restudy of the first 1400 tumors in the Bladder Tumor Registry. Personal communication.

[6] Friedman, M., and Lewis, L. G.: A new technic for the radium treatment of carcinoma of the bladder. Radiology, **53**: 342, 1949.

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THE NONOPERATIVE TREATMENT OF STRESS INCONTINENCE IN WOMEN

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Stress incontinence has been attracting an increasing amount of attention among gynecologists and female urologists in recent years. This is due probably to the frequency of the condition and the inconvenience it causes. One can gain an idea of the current interest in this problem by glancing at the programs of our medical societies or from the statement of Marchetti (personal communication, 1952) that he has found in the literature "approximately 95" surgical procedures designed to correct this condition.

The multiplicity of these procedures does not, in my experience, indicate that the surgical treatment is completely unreliable. My results with the Kelly plication of the vesical sphincter have generally been very satisfactory; and this experience has been supported by TeLinde who recently summarized our results in 249 cases in which this procedure had been used between 1937 and 1947. He reported that 90.3 per cent had been cured, 5 per cent improved and 3.5 per cent failed, with 1.2 per cent untraceable. This has probably not been the universal experience; otherwise the many other procedures would not have been devised. As matters stand today, no surgical procedure has proved completely satisfactory, because of persisting incontinence or unfavorable complications and sequelae which may be more disturbing than the original complaint.

In 1951, an entirely new idea was introduced into this problem, when Kegel reported that stress incontinence could be benefited by simple exercises designed to strengthen the sphincter muscles of the urethra, without any surgical operation whatever. This report stimulated me to assemble my own experience in the nonoperative treatment of this condition and analyse the various factors that seem to contribute to its cause or cure.

The present communication is a summary of these findings. It is based on the study of 26 cases, all but 2 of whom I have studied and treated personally since January 1951. All of these patients have been studied medically, gynecologically and when necessary, urologically, in the effort to determine the causative factors in each case, and the methods of treatment which seemed to offer the best chance of cure.

CLINICAL DATA

Age. In our experience, stress incontinence occurs most frequently in women above the age of 40 years. Some of our patients, however, have stated that it troubled them even in adolescence. Our oldest patient is 91 years old.

Parity. In this series, 22 of 26 were multiparae; 4 were nulliparous. One of our

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most severe cases of stress incontinence is in a virgin, 75 years old, who has had this ailment for 21 years.

Duration of symptoms. There is nothing striking about this feature. There were about the same number in all categories, those who had suffered for 5, 10, 15 years or longer. In our experience, this is merely a measure of the patience of the individual, the success or failure of past treatment and an indication that in most cases stress incontinence persists until adequate treatment is instituted

Associated genital prolapse and cystocele. Complete or second degree prolapse was present in six, and there was a slight or moderate relaxation of the anterior vaginal wall in four. In about 40 per cent, therefore, there was obvious lack of support of the bladder and urethra; in these cases it was the result of childbirth injury. The relationship between stress incontinence and prolapse will be discussed in connection with treatment.

Associated urological disorders. In 10 cases, there were associated urinary disorders as follows:

Associated Urinary Disorders

	CASES	UROLOGIC RESULT
Hydronephrosis	1	Not treated
Recurrent pyelitis, infected hydronephrosis	2	1 cured, 1 improved
Trigonitis, urethritis	6	cured
Urethral caruncle	1	cured
Chronic cystitis	2	cured

In only two of these was the urinary condition the chief complaint, the 2 cases of recurrent pyelitis and infected hydronephrosis. One of these was cured urologically, the other was improved. The patient with a minor degree of asymptomatic hydronephrosis was not treated urologically; her only complaint was stress incontinence of which she was relieved by exercises. The remaining cases of trigonitis, urethritis, cystitis and urethral caruncle were treated urologically with satisfactory results. The effect of eliminating these urological disorders on stress incontinence was not as satisfactory, for only 3 patients noticed any benefit as far as urinary control was concerned.

Obesity. This is one of the commonest findings in women with stress incontinence. Two-thirds of our cases showed either marked or moderate obesity.

Cough. A severe and intractable cough, especially in an elderly, obese woman, may be an insurmountable handicap in treating stress incontinence. This was the situation in two of our cases. One of these patients had been completely cured of rectal incontinence by suture of the sphincter ani, and greatly relieved of urinary incontinence by an operation for second degree prolapse and suture of the vesical sphincter. Seven years later, an intractable, asthmatic cough developed with the result that both rectal and urinary sphincters gave way and incontinence returned. Another patient, who had been considerably relieved by exercises, likewise had a recurrence of urinary incontinence as the result of an uncontrollable cough.

Postoperative stress incontinence. In this series, there are two who did not have stress incontinence till after a gynecological operation. Both had vaginal hysterectomy for uterine prolapse. In the first patient stress incontinence developed after the performance of a vaginal hysterectomy by a capable gynecologist in 1938; it persisted after a second operation in 1948, when the vesical sphincter was tightened, likewise by an excellent gynecologist. This patient still has stress incontinence, refusing so far to go to the trouble of trying any exercises.

In the second patient stress incontinence developed in 1930, after a vaginal hysterectomy for prolapse. The stress incontinence lasted one year when it disappeared spontaneously. Shortly after that the prolapse recurred, although the urinary control remained perfect. In 1949, I operated upon her for the vaginal prolapse, and again the stress incontinence returned. After one year, without any treatment at all, the incontinence disappeared. So far, the prolapse has not recurred.

Various theories have been given to explain the development of stress incontinence after gynecological operations, especially those for prolapse. Similar experiences have been reported by Jones and Kegel, TeLinde and Kennedy. Counseller attributes it to failure to elevate the urethra and vesical neck, especially in "patients with prolapse and large cystoceles." Kennedy attributes it to scar formation around the urethra and vesical neck, which prevents the proper function of the vesical sphincter. It seems difficult to explain this type of stress incontinence without theorizing unduly. It is not always an irreparable type of weakness, however; indeed, in our two cases, one disappeared completely without treatment, and in another, the incontinence became better with rest. This would rather indicate that in these two cases there was a temporary interference with the sphincter mechanism, possibly an injury either to the nerves or muscles.

Other operative procedures had been performed on eight of these women, without any effect on the stress incontinence, as follows:

	CASES
Kelly plication of vesical sphincter	2
Abdominal hysterectomy for myoma	1
Abdominal hysterectomy and perineal repair for prolapse and myoma ...	1
Repair of cystocele and rectocele	2
Repair of vaginal prolapse	1
Abdominal suspension of uterus and advancement of the bladder	1
Vaginal hysterectomy for prolapse	2

In only two of these was there any direct effort to strengthen the sphincter muscles. In the others, for various reasons, the operators made no attempt to strengthen the urethral sphincters, apparently trusting that the correction of gross pressure faults would relieve the stress incontinence. In none of these cases was the incontinence corrected.

This experience is rather contrary to the opinion often expressed that the adequate correction of a large cystocele or prolapse will automatically restore normal vesical control. This is probably quite true in certain instances; however, the above experience suggests that one cannot always rely on such an eventuality.

The above analysis of the clinical data in this series indicates that stress incontinence occurs in a variety of circumstances, and that it is difficult to attribute it to any one factor. It occurs in the young and old, nulliparous and parous, *independently* of any other urinary disorder, in the fat and thin, in the presence of senility and neurological disorders, postoperatively and without respect to any other gynecological disorder.

In view of this and in the absence of any single causative disorder, it seems reasonable to accept the general theory that the sphincter mechanism in women is not particularly rugged, and that its efficiency may be easily impaired by any factors that increase the pressure or stress on the full bladder or impair the neuromuscular mechanism of urinary control.

TREATMENT

In these 26 cases, the following treatment was carried out, with the following results:

	CASES	RESULT		
		Cured	Improved	Failed
No treatment	3	1		2
Cystoscopy	6	2	3	1
Weight reduction	2		2	
Exercises	19	6	5	4

In four additional patients, exercises have been used too recently to warrant any conclusions.

NO TREATMENT

Three patients received no treatment at all. They are included because in one of them, the stress incontinence disappeared spontaneously. In the other two, there has been no improvement at all. For one reason or another, they have refused to try the exercises we have recommended. However, the spontaneous cessation of incontinence in one instance without any treatment whatever, shows that observation and conservative treatment may be advisable at times before performing an extensive plastic operation.

CYSTOSCOPIC TREATMENT AND STRESS INCONTINENCE

We shall analyse this problem in relation to the particular urologic disorder. *Slight hydronephrosis and hydro-ureter*, without infection and asymptomatic, was present in one case of stress incontinence. We paid no attention to the urologic finding. The stress incontinence was treated by exercises, with complete relief.

Infected hydronephrosis with recurring pyelitis was the chief complaint of 2 patients with stress incontinence. In one, the urinary disorder yielded promptly to ureteral dilatations and chemotherapy; and, without any other treatment, the stress incontinence disappeared at the same time. In the second case, the urinary lesions were much more severe; for 16 years there had been recurring attacks of pyelitis, three or four times a year, with pain, fever and incapacitation. Stress incontinence had also been present for more than 20 years. After a year of ureteral dilatations and chemotherapy, the urinary infection was controlled, and there have been no further attacks during the past year. However, the stress incontinence has been unaffected. This patient began exercises too recently to warrant drawing any conclusions.

Trigonitis and urethritis were treated in six persons with stress incontinence. In three, the only treatment was local applications to the urethra and trigone, with urethral dilatations; of these three, two were relieved of stress incontinence and one was not. Three other patients received urologic treatment plus exercises; two were cured and one was relieved of stress incontinence.

Chronic cystitis. We have had two elderly women with stress incontinence and also chronic cystitis. Although the cystitis was apparently eliminated in both instances, with resulting clear and sterile urine, the stress incontinence has not been relieved at all. Furthermore, both of these women have tried exercises without any benefit. In these cases, it appears to us that the failure to cure the stress incontinence is due to a cumulation of handicaps,—age, both being over 75 years old; long duration of incontinence, more than 20 years; senile changes, and in one case progressive neurologic changes involving the legs and probably the anal and rectal sphincters. These factors, as Kegel has indicated, nullify almost any effort to treat urinary incontinence.

Urethral caruncle was found and removed in one patient with stress incontinence, without any effect on the urinary control. Subsequently, the stress incontinence was cured by exercises.

From this experience, it seems that it is worth while to eliminate urologic disorders in treating stress incontinence by exercises. In a few instances, the urologic treatment may benefit the urinary control; in others, although it may not relieve the stress incontinence, it may improve the general health and comfort and enable one to appraise more accurately the vesical function.

WEIGHT REDUCTION

In our experience, obesity is found very frequently in women with stress incontinence. Although we always advise obese patients to try to reduce their weight, such advice is seldom followed. In two instances, however, weight reduction was successful and seemed to play a part in overcoming stress incontinence. In one such case, the only other therapy was the local treatment of a very mild urethritis and trigonitis.

EXERCISES

Exercises were used exclusively or as the chief therapy in 19 patients, and in fifteen of these, enough time has passed to warrant drawing conclusions. Six have been cured, five have been improved, and four have not been noticeably benefited.

The exercises consist solely in the voluntary tightening of the vesical and rectal sphincters, as recommended by Kegel. The patient is told to contract the vesical sphincter just as if she were trying to prevent the escape of urine; at the same time she is to contract the rectal sphincter as if she were trying to prevent the escape of gas or fecal material.

It is important that the patient should understand this clearly and perform the exercises accurately and thoroughly. In my experience, one can explain these exercises clearly by simple verbal directions, without demonstrating these muscles on an examining table or having the patient contract the vagina on the examiner's finger.

Also, I have not used the perimeometer that has heretofore been a part of this therapy. It seemed a needless encumbrance that might even make it inconvenient or impossible for some persons to carry out the exercises regularly. In these particulars, our methods have eliminated some office procedures and demonstrations and have omitted the use of a rather cumbersome and expensive instrument.

We instruct our patients to carry out these contraction exercises 15 times in the morning, noon and night, and as many times in addition as she desires, at least 45 times every day. Being unencumbered by any apparatus, she can contract the muscles at any time or place.

Results. In 15 persons in whom the results are reliable, six have been cured of stress incontinence, five improved and four failures. An analysis of the histories of those who were cured or greatly improved by exercises yields certain interesting data.

As regards *age*, they were evenly distributed between the ages of 40 and 70. Two were nulliparous, the rest parous. Two had urethritis and trigonitis, for which they were treated also. In over half of these, the stress incontinence had been present more than 10 years.

Three of these patients had had well-executed plastic operations for the cure of various types of childbirth injury. Two had complete vaginal and uterine prolapse, one a large rectocele with descensus. In none was any specific operation performed upon the sphincters of the bladder and urethra, although all had stress incontinence before these operations. All of these operations were done by excellent gynecologists, and in every case the childbirth injury was perfectly corrected. However, in not one case did the operation have any effect on the stress incontinence.

These patients remained incontinent for varying lengths of time after these operations, from 1 to 23 years. All subsequently obtained complete urinary control by exercises.

It has often been stated that if, in a case of prolapse or cystocele, one restores the normal anatomical relationships of the pelvic organs, cures the prolapse and elevates the urethra and bladder to their proper level in the pelvis, such procedures would generally correct stress incontinence. Although this proposition may be true at times, our experience has shown that one cannot always depend upon it.

Length of treatment. In the average case, improvement in urinary control is noted within one month after beginning exercises. Some women are satisfied with this result and then stop their exercises. In our experience, the shortest time needed to eliminate stress incontinence completely has been 2 weeks; this patient had had incontinence for only 6 months.

Occasionally, after only a short course of exercises, the incontinence may tend to return; it may again be corrected by resuming the exercises.

Failures. In this group of cases, there are four who received little or no benefit from exercies. A study of these failures brings out certain facts clearly. In the first place, two of these women were quite elderly, 79 and 90 years. The youngest was 57 years old. They were all obese and had had stress incontinence for over 20 years. The oldest of the three, 90 years old, was definitely an invalid with senile changes and did not see much use in trying to improve her situation. She tried the exercises only for about two or three weeks, spasmodically, and then stopped, maintaining that they did no good. Her nurse, however, stated that she felt sure that the patient's clothing was not continually wet, as it had been.

One of the others, 79 years old, made a sincere effort to carry out the exercises. However, she had a progressive neurological disorder that involved not only the legs but also the urinary and rectal sphincters. Furthermore, the fact that a former operation for urinary incontinence, performed almost 25 years previously, had failed, did not give her any encouragement. In this case, the situation seemed rather hopeless from the start, and exercises produced no improvement in either rectal or urinary control.

In the third case, a woman 57 years old, who had had both rectal and urinary incontinence for at least 20 years, the situation was slightly different. In 1941, I performed an operation for cystocele, including also a Kelly plication of the vesical sphincter and also suture of the anal sphincters for a complete perineal tear. Rectal control was immediately restored. Urinary continence, however, returned slowly and never became perfect. After about 6 years, the patient commenced to get very obese, developed a severe, chronic cough that could not be controlled by any medical therapy, and also showed mental and neurological deterioration. After a short time, both the rectal and urinary incontinence returned, and the patient now spends a large part of her time in an institution for nervous disorders. Exercises were tried when the stress incontinence began to return, but with the nervous instability, the severe, hacking cough and obesity, there was no improvement.

The fourth failure was noted in an elderly spinster, 76 years old. She had chronic cystitis and for perhaps 30 years, stress incontinence which had become progressively more severe. With all of this, she was a very intelligent and capable woman, occupying an important executive position. Nothing has relieved the stress incontinence: elimination of the urinary infection, weight reduction or faithful use of exercises. This patient has always refused any surgical attempt to correct the incontinence.

In summary, then, we might classify the factors in these failures as follows: Advanced age, long duration of stress incontinence, senility, obesity, neurological disorders, severe cough, failure to continue exercises long enough to obtain relief.

In our experience, advanced age, long duration of stress incontinence and obesity are not insurpassable hindrances. However, in the presence of a severe, chronic cough, senility and progressive neurological disorders, the outlook is usually unfavorable.

CONCLUSIONS

In the management of 26 cases of stress incontinence in women, we have had the following experiences:

Stress incontinence has been cured or remarkably relieved in some cases by cystoscopic elimination of local urological disorders such as trigonitis, urethritis, hydro-ureter and hydronephrosis. In other instances, such urological treatment had no effect on the poor vesical control. Also, in one instance, stress incontinence of one year's duration disappeared spontaneously without any treatment at all. Reduction of obesity has been a useful adjunct in any form of therapy.

Exercises designed to strengthen the sphincters of the urethra and rectum and to increase the strength of the vaginal and perineal muscles, either cured or greatly relieved almost 75 per cent of those who tried them. The average patient reported relief or cure after using the exercises one month. In one instance, complete urinary control was acquired in two weeks. We have not found it necessary to use any mechanical device, such as a perineometer.

Failures have occurred in the presence of senility, neurological disorders affecting the vesical and rectal sphincters or severe and incurable cough. The long duration of the incontinence has not in itself had a bad prognostic value, except when it may be accompanied by very advanced years, senility or degenerative neurological processes.

Stress incontinence is not always present in women with gross mechanical faults, such as complete prolapse of the uterus or vagina in which the entire base of the baldder and urethra lie outside the vagina. We have seen it often in women without any demonstrable mechanical displacement of the bladder or urethra. Likewise, it has persisted in women after successful correction of complete prolapse and in them has been subsequently cured by exercises.

These data suggest to us that stress incontinence may be produced by a variety of factors, as we have indicated. The fact that 90 per cent have been cured after plication of the vesical sphincter, and that almost 75 per cent have been cured or improved by simple exercises suggests that urinary control basically depends upon the state of the sphincter mechanism. A strong vesical sphincter can function properly even in the presence of complete genital prolapse, whereas a weak sphincter produces incontinence even in a virgin.

This study has shown that the best results in the treatment of stress incontinence are obtained by careful medical, gynecological and urological study of each case, as indicated, discovering and treating adequately every factor that might interfere with the normal function of the urethral and vesical sphincters.

In conclusion, the nonoperative treatment of stress incontinence in women has opened a new chapter in the management of this condition. If stress incontinence is accompanied by gross gynecological disorders that in themselves require surgical treatment such as prolapse of the uterus or vagina or large pelvic tumors, these gross disorders should be corrected by appropriate surgical means. At the same time, if feasible, a Kelly plication of the vesical sphincter should be done. When, however, there is no significant gynecological or urological disorder, the stress incontinence should be treated as we have suggested, by exercises designed to strengthen the sphincter mechanism and accessory medical or urological care as indicated.

If stress incontinence persists after an operation for genital prolapse with or without plication of the vesical sphincter, the chances are excellent that, in the absence of senility, neurological disease or other unfavorable complications, normal urinary control may be obtained by the use of simple exercises.

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NON-SURGICAL MANAGEMENT OF CONGENITAL NEUROGENIC VESICAL DYSFUNCTION

CHARLES L. PRINCE AND PETER L. SCARDINO

Myelodysplasia and spina bifida are often the cause of grave and frequently fatal urinary tract disorders in children. Aside from the urinary tract disease, other characteristic findings present are rectal incontinence, severe motor and sensory changes of the lower extremities, club feet, and hydrocephalus. The high mortality and brief life span frequently noted in these cases are chiefly due to the urinary tract complications. Neurogenic bladder with urinary incontinence, ureteral dilatation, hydronephrosis and urinary infection inevitably lead to gradual decrease in renal function and uremia, when improperly managed. To quote Campbell: "The clinical course of the inadequately treated child is . . . with rare exception, progressively down grade. The child may live for years but rarely into early adulthood; progressive renal injury and the resulting toxemia commonly kills these patients in early childhood and only comparatively few reach the tenth year." There is surprisingly little reference in the literature to the management of this very important condition. The primary therapeutic aims in these cases are 1) eradication and prevention of urinary infection, 2) the elimination of residual urine, 3) the prevention and improvement of renal damage, and 4) the establishment of as normal urinary function as is possible. To these ends, the chief methods of management recommended have been permanent suprapubic cystostomy,[1, 2] transurethral resection of the vesical neck,[3, 4] and to a lesser degree, bilateral nephrostomy. Cystostomy and nephrostomy are inconvenient, messy, and difficult to manage in children. With permanent catheters, infection is inevitable and stone formation is a frequent complication. The results following transurethral resection of the vesical neck have been far from satisfactory in accomplishing the desired end-results.[4]

We have followed two severe cases of this type over a period of several years. They have been managed conservatively, without surgery of any type, and the results have been extremely gratifying. Infection and residual urine have been eliminated in both instances. Incontinence in one case has completely disappeared, and is satisfactorily controlled in the other. In both instances there has been almost unbelievable improvement in the upper urinary tract dilatation, and restoration of renal function to normal. These cases are presented in the hope that more of these children will be handled in this fashion.

Accepted for publication June 6, 1952.

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[4] Emmett, J. L. and Helmholz, H. F.: Transurethral resection of the vesical neck in infants and children. J. Urol., 61: 463, 1948.

CASE REPORTS

Case 1. M. C., a 5 year old boy, was first seen July 9, 1947 experiencing urinary and fecal incontinence, pyuria with recurrent episodes of chills and fever, and bilateral flank pain. A myelomeningocelectomy had been performed several days after birth. Examination revealed a bright male child who was fairly well developed. There was no hydrocephalus. A well healed incision was found in the midline over the lumbosacral region. Marked motor and sensory changes were present in both lower extremities, with bilateral talipes equinovarus. The patient could neither walk nor stand. A large area of complete saddle anesthesia was present.

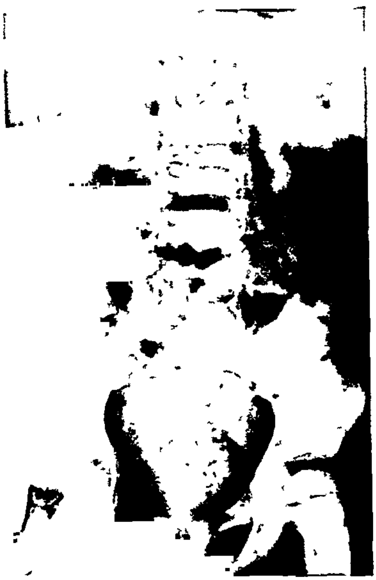

FIG. 1

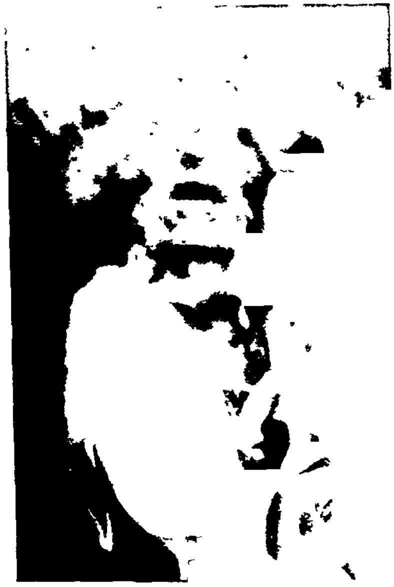

FIG. 2

FIG. 1. Case 1. Excretory urogram (7/10/47), 50 minute post injection film showing marked bilateral hydronephrosis and delayed function.

FIG. 2. Case 1. Injection cystogram (7/10/47) showing megalobladder with reflux on left demonstrating ureteral dilatation and tortuosity and hydronephrosis. Funneling of vesical neck and prostatic urethra is present.

The rectal sphincter was atonic. The bladder was distended almost to the umbilicus, and urine dribbled constantly from the penis. Moderate suprapubic pressure caused flow of urine from the penis with good force. Residual urine was 175 cc. The urine showed 10–15 white blood cells per high power field and a faint trace of albumin. It was otherwise negative. Culture of the urine revealed E. coli. A plain urogram showed no evidence of stone in the urinary tract. There was spina bifida involving the last three lumbar vertebrae and sacrum. An excretory urogram revealed moderate enlargement of both kidneys with delayed excretion of the contrast medium. Not until 50 minutes after injection was there good filling of the kidneys. The right ureter and bladder were not visualized. The left ureter was visualized only in its upper part. There was bilateral hydronephrosis (fig. 1). Injection cystogram (fig. 2) showed a megalobladder pointing somewhat to the right and a widely funneled vesical neck and prostatic urethra. There was reflux on the left, completely filling the left ureter and kidney. The former was markedly dilated and tortuous. There was grade 2 pyelectasis and caliectasis. There was no reflux on the right side. Blood nonprotein nitrogen was 35 mg. per cent. The phenolsulfonphthalein test showed 50 per cent excretion in 2 hours. The situation was thoroughly discussed with the mother who was extremely intelligent, willing and cooperative. She was taught to empty the patient's bladder completely by suprapubic manual pressure, and was advised to do this religiously on a schedule of every 2 hours during the day and every 4 hours at night. This she did faithfully. The child was also given an infant size Cunningham penis clamp to wear between voidings and at night to prevent wetting. During the first 18 months of observation there were several flare-ups of urinary infection, all of which responded satisfactorily to sulfonamides, streptomycin, and mandelic acid. Since January 1949, numerous specimens of urine examined have shown no evidence of infection, and all urine cultures have been sterile. For the last 2 years the child has not worn the penis clamp. He never wets himself during the day, and rarely wets the bed at night. He has learned to empty his bladder completely without help, using the abdominal muscles and manual suprapubic pressure. He has been checked several times by catheterization immediately after voiding

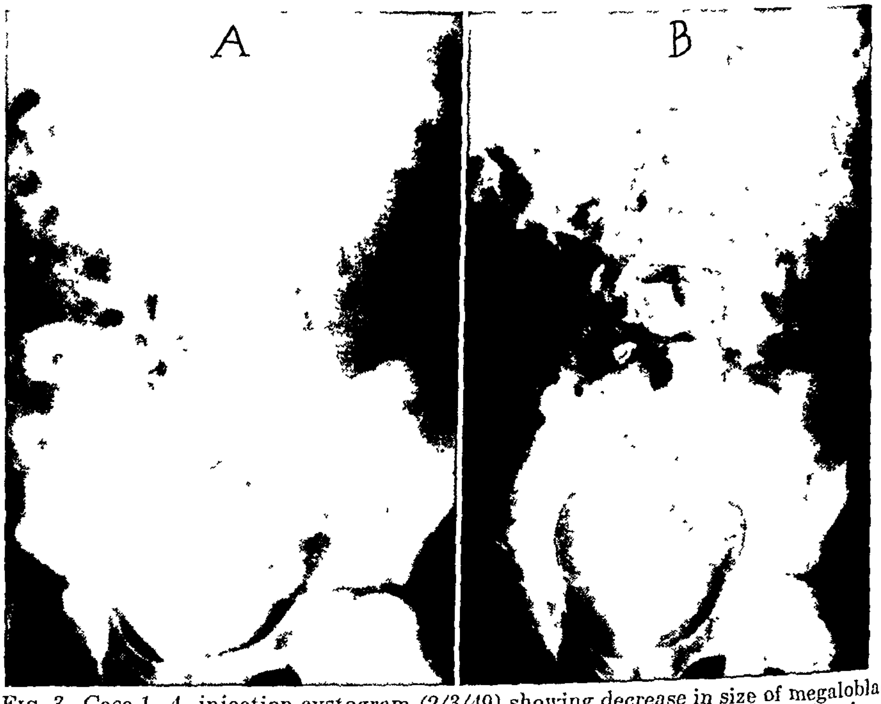

FIG. 3. Case 1. *A*, injection cystogram (2/3/49) showing decrease in size of megalobladder, reduction in ureteral dilatation and tortuosity, and decrease in hydronephrosis. *B*, excretory urogram (4/14/52), 15 minute post injection film showing normal function with marked improvement in hydronephrosis and lessening of ureteral dilatation and tortuosity.

and there is no residual urine. The child is now 10 years of age and the improvement in general well-being, appearance and weight has been most gratifying. The talipes has been corrected orthopedically. With the aid of leg braces and crutches, he gets about amazingly well. He is doing well in school. Excretory urograms and cystograms have been made at intervals. Injection cystogram made February 3, 1949 (fig. 3, *A*) showed reduction in size of the bladder. The bladder outline remained irregular but the vesical neck and prostatic urethra were funneled. There was still reflux filling the entire the entire left ureter and kidney. There was considerable reduction in the pyelo-ureterectasis, and decrease in the tortuosity of the ureter. Excretory urograms made September 29, 1951, somewhat over 4 years after treatment was begun, showed great improvement. These films show prompt excretion of the contrast medium and good filling of both kidneys 5 minutes after injection indicating marked improvement in renal function. The 15 minute post injection film (fig. 3, *B*) shows excellent filling of both kidneys and both lower ureters. The left kidney is now within normal limits. There remains slight pyelectasis and caliectasis on the right, but improvement has been marked. There is still slight dilatation and tortuosity of both lower ureters. A cystogram (fig. 4) made April 14, 1952 shows excellent filling of the bladder, the outline of which is still somewhat irregular. However, there is now no reflux of contrast medium into the left kidney.

Case 2. H. A., a boy, aged 4 years, was first seen April 22, 1949. He had been completely incontinent since birth. During the month prior to his first visit he had had three episodes of pyuria with chills, fever, burning on urination, and pain in the right renal area. The episodes of infection had responded temporarily to sulfonamides and penicillin, but had recurred promptly. Past history revealed the presence of a large myelomeningocele at birth, which was removed and closed surgically at the age of 2 weeks. He had never learned to stand or walk because of partial paralysis of the lower extremities. Enlargement of the head increased after birth until the age of 3½ years. At this time, the fontanelles apparently closed and the hydrocephalus became stationary. However, the child was very bright and talkative. Examination revealed a fairly well developed boy, with no control over his lower extremities. The head was judged to be about 50 per cent larger than normal, with typical hydrocephalic contours. There was a flat healed incision in the midline of the lumbosacral area without prominence. Sensory and motor loss appeared complete below the knees and were variable from the waist to the knees. There was bilateral talipes equinovalgus. A large area of typical saddle anesthesia was present. The rectal sphincter was flaccid. The bladder was palpable to the level of the umbilicus. The right kidney was readily palpable, somewhat enlarged, and tender. There was no tenderness over the left renal area. Residual urine was 200 cc. Very little suprapubic pressure was required to cause escape of urine from the penis with a flow of good size and force. The urine showed a trace of albumin and 35–40 white blood cells per high power field. Otherwise the urine was negative. Culture of the urine revealed non-hemolytic Staphylococcus aureus. Blood nonprotein nitrogen was 40 mg. per cent. A plain urogram showed no calculus in the urinary tract. There was spina bifida involving sis (fig. 1). Injection cystogram (fig. 2) showed a megalobladder pointing somewhat to the right and a widely funneled vesical neck and prostatic urethra. There was reflux on the left, completely filling the left ureter and kidney. The former was markedly dilated and tortuous. There was grade 2 pyelectasis and caliectasis. There was no reflux on the right side. Blood nonprotein nitrogen was 35 mg. per cent. The phenolsulfonphthalein test showed 50 per cent excretion in 2 hours. The situation was thoroughly discussed with the mother who was extremely intelligent, willing and cooperative. She was taught to empty the patient's bladder completely by suprapubic manual pressure, and was advised to do this religiously on a schedule of every 2 hours during the day and every 4 hours at night. This she did faithfully. The child was also given an infant size Cunningham penis clamp to wear between voidings and at night to prevent wetting. During the first 18 months of observation there were several flare-ups of urinary infection, all of which responded satisfactorily to sulfonamides, streptomycin, and mandelic acid. Since January 1949, numerous specimens of urine examined have shown no evidence of infection, and all urine cultures have been sterile. For the last 2 years the child has not worn the penis clamp. He never wets himself during the day, and rarely wets the bed at night. He has learned to empty his bladder completely without help, using the abdominal muscles and manual suprapubic pressure. He has been checked several times by catheterization immediately after voiding

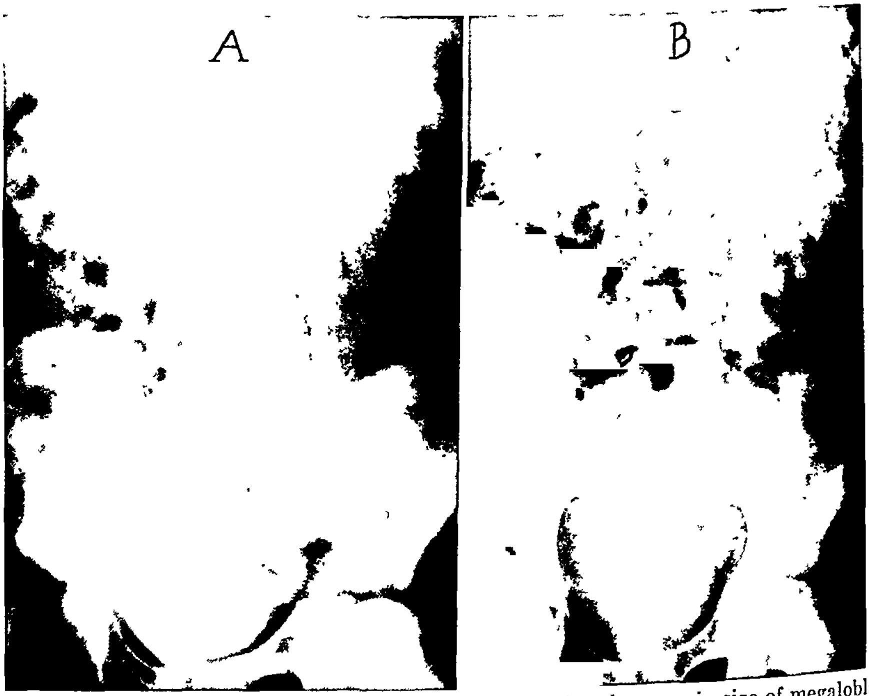

FIG. 3. Case 1. *A*, injection cystogram (2/3/49) showing decrease in size of megalobladder, reduction in ureteral dilatation and tortuosity, and decrease in hydronephrosis. *B*, excretory urogram (4/14/52), 15 minute post injection film showing normal function with marked improvement in hydronephrosis and lessening of ureteral dilatation and tortuosity.

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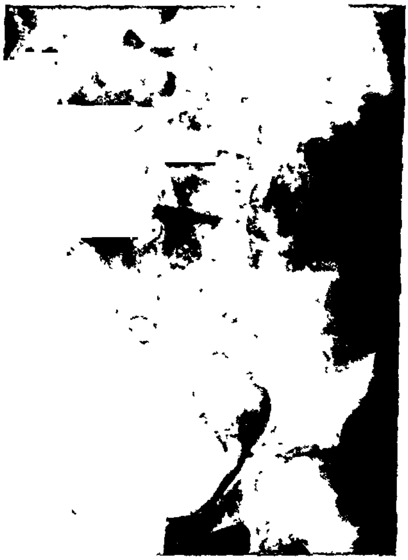

FIG. 4

FIG. 5

FIG. 4. Case 1. Injection cystogram (4/14/52) showing absence of reflux on left side.
FIG. 5. Case 2. Injection cystogram (4/22/49) showing meaglobladder, funneling of vesical neck and reflux on right with marked ureteropyelectasis and ureteral tortuosity.

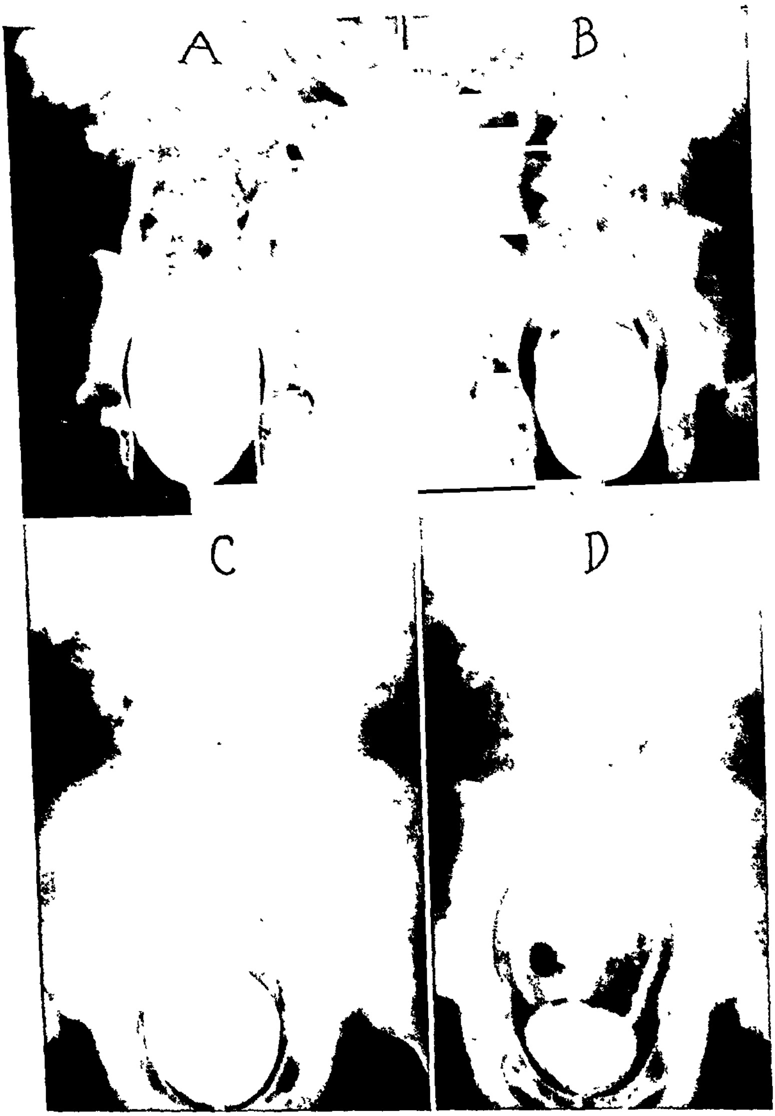

FIG. 6. Case 2. *A*, injection cystogram (6/8/50) showing bilateral reflux with marked reduction in size of hydronephrosis and hydro-ureter. *B*, injection cystogram (6/29/51) showing decrease in size of megalobladder. Bilateral reflux persists but hydronephrosis has disappeared and ureteral dilatation and tortuosity are almost gone. *C*, cystogram (1/21/52) showing further reduction in size of megalobladder and absence of reflux. *D*, excretory urogram (1/21/52) 15 minute post injection film showing normal function and normal kidneys and ureters.

ureters are only slightly dilated, and the tortuosity has disappeared. The renal pelves and calyces are now almost within normal limits. After 3 years an injection cystogram (fig. 6, *C*) shows marked reduction in size of the megalobladder. Reflux is no longer present. The excretory urogram shows an essentially normal upper the last lumbar vertebra and the sacral segments. The injection cystogram (fig. 5) showed a megalobladder with a smooth outline. There was funneling of the vesical neck and prostatic urethra. There was reflux of contrast medium completely filling the right ureter and kidney, without reflux on the left. The entire right ureter was tremendously dilated and tortuous, and measured 2.2 cm. at its widest point. There was grade 3 pyelectasis and caliectasis. An excretory urogram showed good concentration of contrast medium in both kidneys and ureters 25 minutes after injection, with dilatation of the left kidney and ureter equal to that of the right. This child was started on a regimen identical with that of the first patient. The parents were taught to empty the bladder by suprapubic pressure every 2 hours during the day and every 4 hours at night. The child was given a small Cunningham penis clamp to control the urinary incontinence. He was immediately hospitalized and given large doses of penicillin. The urine became free of pus and sterile on culture. This child has had only one subsequent flare-up of urinary infection, which occurred 1 month after his original visit. This episode also responded promptly to penicillin. It has now been over three years since he has had any urinary infection. Repeat cystograms, made 1 year (fig. 6, *A*), 2 years (fig. 6, *B*), and 3 years (fig. 6, *C*), after the instigation of treatment have shown steady and almost unbelievable improvement in the upper urinary tract on each side. Figure 6, *A* shows the result of 1 year's treatment. There is reflux up both sides, but there has been marked lessening of the ureteral dilatation and tortuosity and great improvement in the hydronephrosis. At the end of 2 years (fig. 6, *B*) the improvement is even more striking. While bilateral reflux exists, the

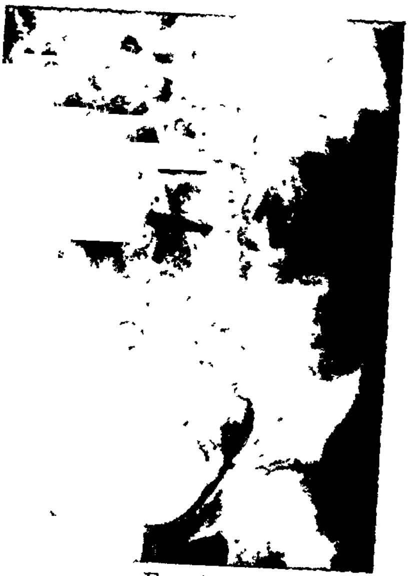

FIG. 4

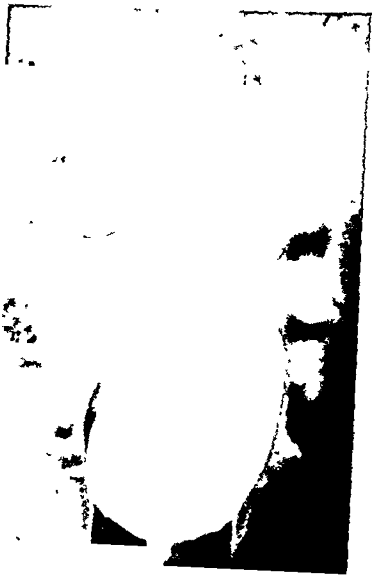

FIG. 5

FIG. 4. Case 1. Injection cystogram (4/14/52) showing absence of reflux on left side

FIG. 5. Case 2. Injection cystogram (4/22/49) showing meaglobladder, funneling of vesical neck and reflux on right with marked ureteropyelectasis and ureteral tortuosity.

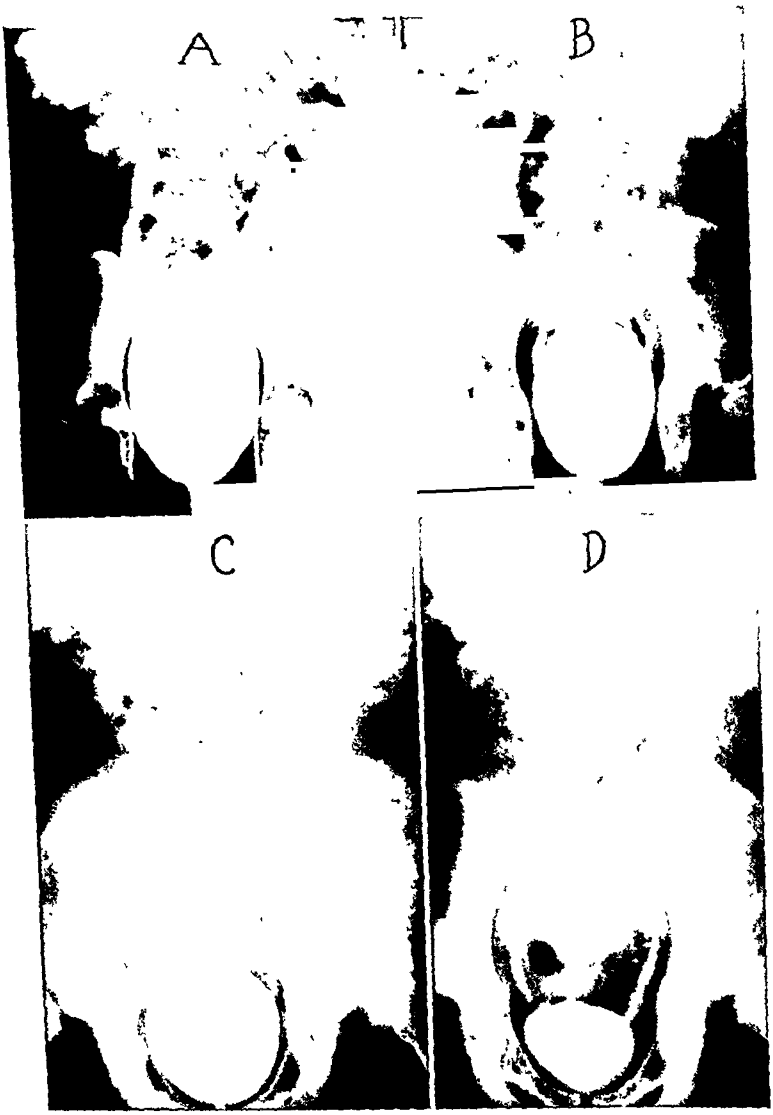

FIG. 6. Case 2. *A*, injection cystogram (6/8/50) showing bilateral reflux with marked reduction in size of hydronephrosis and hydro-ureter. *B*, injection cystogram (6/29/51) showing decrease in size of megalobladder. Bilateral reflux persists but hydronephrosis has disappeared and ureteral dilatation and tortuosity are almost gone. *C*, cystogram (4/21/52) showing further reduction in size of megalobladder and absence of reflux. *D*, excretory urogram (4/21/52) 15 minute post injection film showing normal function and normal kidneys and ureters.

ureters are only slightly dilated, and the tortuosity has disappeared. The renal pelves and calyces are now almost within normal limits. After 3 years an injection cystogram (fig. 6, *C*) shows marked reduction in size of the megalobladder. Reflux is no longer present. The excretory urogram shows an essentially normal upper urinary tract, with normal function (fig. 6 *D*). This child is now 7 years old and has made impressive gain in general health, appearance, and weight. He gets about well with the aid of lower leg braces and crutches. He is doing extremely well in school. This child, too, has learned to empty the bladder without assistance by suprapubic pressure at regular 2 hour intervals. That he is able to empty completely has been proven by immediate catheterization after voiding. He still wears the penis clamp during the day because of persistent mild incontinence between voidings. He does not wear the penis clamp at night, however, and very rarely wets the bed.

DISCUSSION

We were determined to manage the 2 cases presented herein conservatively if possible, without permanent suprapubic drainage. This seemed feasible, as in each instance very little suprapubic pressure was required to empty the bladder with a good flow, indicating little or no vesical neck and urethral resistance. Absence of obstruction at the vesical neck was further demonstrated in both cases by funneling of the vesical neck and prostatic urethra on cystogram. In the absence of demonstrable vesical neck obstruction transurethral resection was felt to be unnecessary. Thompson and Jacobson state that vesical neck obstruction, usually in the form of a spastic internal sphincter, is present in most instances of neurogenic vesical dysfunction resulting from spina bifida. They have, therefore, suggested transurethral resection of the vesical neck almost to the exclusion of any other method of treatment. Their best results were obtained in cases in which symptoms were of comparatively recent onset, or those in which there was minimal damage to the urinary tract. Their poorest results were obtained in those cases in which there were prolonged symptoms and extensive damage to the upper urinary tract. Emmett and Helmholz reported 18 cases of vesical dysfunction from myelodysplasia and spina bifida in which transurethral resection of the vesical neck was carried out. In only five of their cases was upper tract dilatation demonstrated. They found only one third of these cases to be completely relieved of symptoms, and state that in this group the operative results were far from satisfactory. In neither of these series was there mention of the late effects of operation on the upper urinary tract. In these cases, when vesical neck obstruction can be demonstrated by cystogram and panendoscopy, transurethral resection is certainly indicated, and is frequently very helpful in establishing more normal voiding and eliminating residual urine. McCarroll[5] made an excellent study of urinary incontinence due to spina bifida a number of years ago, and showed that great improvement in urinary control could be obtained by conservative measures, chiefly bladder re-education. In his experience the cases with a spastic internal sphincter and relaxed bladder wall showed most improvement under conservative therapy. It is now generally felt that this type case should have transurethral resection of the vesical neck. McCarroll made no mention whatever of the more serious upper urinary complications in spina bifida.

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[5] McCarroll, H. R.: Spina bifida urinary incontinence. Surg. Gynec. & Obst., 64: 721, 1937.

We believe that permanent cystostomy or nephrostomy never should be used except when conservative measures and transurethral resection of the vesical neck have failed to eliminate residual urine and infection, except in an occasional rare instance where it may be an emergency or life-saving procedure.

We have demonstrated that with strict adherence to a rigid routine of emptying the bladder regularly by manual suprapubic pressure, and with the aid of proper chemotherapy to control infection, the primary therapeutic aims outlined in the foregoing paragraphs can be met with amazing success. By preventing the bladder from becoming overdistended, and with the eradication of infection, the markedly damaged upper urinary tracts have returned to almost normal limits. Renal function has been restored to normal. In both instances, reflux has been completely abolished. One child has gained perfect urinary control. Both children have learned to completely empty their bladders without assistance.

SUMMARY AND CONCLUSIONS

Spina bifida and myelodysplasia are frequently the cause of severe urinary tract complications in children, resulting in decreased longevity and high mortality. The chief urinary tract complications are neurogenic vesical dysfunction with urinary incontinence, urinary infection, pyelo-ureterectasis, and impaired renal function.

The chief methods of treatment have been permanent suprapubic cystostomy, bilateral nephrostomy, and or transurethral resection of the vesical neck. The first two improve urinary drainage, reduce infection, and improve and prevent renal damage, but are messy and difficult to manage in children. Stone formation is a frequent sequela. Transurethral resection relieves symptoms in about $^1/_3$ of the cases when concomitant vesical neck obstruction is demonstrable, but long range results of this operation and its effect on the damaged upper urinary tract and impaired renal function have never been adequately studied or reported.

Two cases of myelodysplasia and spina bifida with severe urinary tract complications have been presented in detail, with careful clinical follow-up and repeated x-ray studies during the course of treatment. In these 2 cases, surgery was not performed. Careful conservative management with regular emptying of the bladder by suprapubic manual pressure, and control of urinary tract infection has been the only treatment. Infant size penis clamps were used in both cases to control urinary incontinence. In one instance this has been discarded. Both children are now able to empty the bladder completely without aid. In each case there has been no urinary infection for several years. The return of renal function to normal and the disappearance of the hydronephrosis, hydro-ureter and ureteral tortuosity is most remarkable.

The results demonstrated here, obtained by conservative treatment, show that even severe cases of this type can be handled without surgery with gratifying results. It is our belief that these long-term results cannot be matched by any other form of management.

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USEFUL INSTRUMENT IN REPAIR OF VESICOVAGINAL FISTULA

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One of the technical difficulties in the vaginal and transvesical approaches in repair of vesicovaginal fistula is the problem of adequate exposure and mobilization of the operative area. Various devices have been described for use in the repair of this trying complication of gynecological surgery. Hugh Young[1] reported the use of a fenestrated prostatic tractor as an aid in suprapubic repair. Reich and Wilkey[2] report their method of "stringing the fistula" by means of a ureteral catheter passed cystoscopically and brought out vaginally. Both ends were used as a handle to help bring the anterior edge of the fistula closer to the operator and to steady the immediate area of the fistula when making the initial encircling incisions. The use of a cotton twine plug wrapped about the end of a ureteral catheter passed cystoscopically for use in the transvesical approach was described by Miller.[3] Fagerstrom[4] described a ball tractor for use in transvesical repair in which a string was used to bring the vaginally placed ball up against the orifice of the fistula. Obviously this maneuver could not be worked in reverse, i.e. ball in bladder with traction on vaginal string.

More recently, the use of a Foley bag catheter in the vaginal approach has been of real advantage in affording good mobilization of the area of the fistula. Falk and Bunkin[5] give an excellent description of the Latzko operation in 9 successful vaginal repairs. Their article is highly recommended to those faced with the repair of these high-lying fistulas.

They advise the vaginal application of a Foley bag catheter, or Lowsley perineal tractor, through the vaginal aspect of the fistula into the bladder when the fistula is large enough. Traction on the inflated catheter brings the fistula nearer the vaginal outlet and materially helps fix the vaginal vault for incisions and suturing.

In a recent repair of a vesicovaginal fistula resulting from total hysterectomy for fibroids, the operation was considerably simplified by such traction devices. However, since the opening of the fistula would admit neither a Foley catheter nor the Lowlsey perineal retractor, a modification was made of the Foley catheter. Heavy silk was firmly wound and tied to the distal end of the collapsed bag portion of a 22F, 30 cc Foley bag catheter, and the silk end left long. Using a cystoscope, a No. 4 ureteral catheter was passed through the opening of the fistula located above the trigone and retrieved in the vagina by an assistant. The long heavy silk string was then firmly fixed, by several fine silk ties, to the urethral end of the ureteral catheter. The Foley catheter was then passed into the

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[1] Young, H. H.: Surg. Gynec. & Obst., **45**: 226, 1927.
[2] Reich, W. J. and Wilkey, J. L.: Urol. & Cutan. Rev., **47**: 160, 1943.
[3] Miller, C. O.: Urol. & Cutan. Rev., **53**: 83–85, 1949.
[4] Fagerstrom, D. P.: J. Urol., **62**: 717–718, 1949.
[5] Falk, H. C. and Bunkin, I. A.: Surg., Gynec. & Obst., **93**: 404–410, 1951.

bladder and inflated with 25 cc fluid. Traction made upon the vaginal end of the string brought the area of repair (for denudation of the vaginal mucosa with high partial colpocleisis) nearer the vaginal outlet. With the aid of this modified Foley traction the procedure was immeasurably simplified.

The use of this method for fistula openings which do not admit a Foley catheter vaginally is recommended for further trial by those using this particular operative approach. In transvesical repair the reverse application of the same principle will help in a similar fashion.

The urological literature[6, 7] in recent years has stressed the difficulty of the vaginal approach in fistulas after total abdominal hysterectomy. They always occur high in the vault at the junction of the anterior and posterior vaginal walls. Because of the allegedly difficult exposure the transvesical approach has been advocated. The latter approach may be indicated in a particular instance, or even a combined approach might be desirable. However, in fistulas due to total abdominal hysterectomy, the vaginal route would appear to be the most direct. The use of a traction instrument, such as that described herein, episiotomy or Schuchardt incisions, silk stay sutures, and adequate retraction by assistants, will afford good visualization of the operative area. The repair done in this fashion carries a low morbidity and a very high percentage of cure.

67 Chestnut St., Springfield 5, Mass.

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[6] Taylor, W. N.: J. Urol., **60**: 448–492, 1948.
[7] Immergut, S. and Cottler, Z. A.: J. Urol., **63**: 865–871, 1950.

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USEFUL INSTRUMENT IN REPAIR OF VESICOVAGINAL FISTULA

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One of the technical difficulties in the vaginal and transvesical approaches in repair of vesicovaginal fistula is the problem of adequate exposure and mobilization of the operative area. Various devices have been described for use in the repair of this trying complication of gynecological surgery. Hugh Young[1] reported the use of a fenestrated prostatic tractor as an aid in suprapubic repair. Reich and Wilkey[2] report their method of "stringing the fistula" by means of a ureteral catheter passed cystoscopically and brought out vaginally. Both ends were used as a handle to help bring the anterior edge of the fistula closer to the operator and to steady the immediate area of the fistula when making the initial encircling incisions. The use of a cotton twine plug wrapped about the end of a ureteral catheter passed cystoscopically for use in the transvesical approach was described by Miller.[3] Fagerstrom[4] described a ball tractor for use in transvesical repair in which a string was used to bring the vaginally placed ball up against the orifice of the fistula. Obviously this maneuver could not be worked in reverse, i.e. ball in bladder with traction on vaginal string.

More recently, the use of a Foley bag catheter in the vaginal approach has been of real advantage in affording good mobilization of the area of the fistula. Falk and Bunkin[5] give an excellent description of the Latzko operation in 9 successful vaginal repairs. Their article is highly recommended to those faced with the repair of these high-lying fistulas.

They advise the vaginal application of a Foley bag catheter, or Lowsley perineal tractor, through the vaginal aspect of the fistula into the bladder when the fistula is large enough. Traction on the inflated catheter brings the fistula nearer the vaginal outlet and materially helps fix the vaginal vault for incisions and suturing.

In a recent repair of a vesicovaginal fistula resulting from total hysterectomy for fibroids, the operation was considerably simplified by such traction devices. However, since the opening of the fistula would admit neither a Foley catheter nor the Lowlsey perineal retractor, a modification was made of the Foley catheter. Heavy silk was firmly wound and tied to the distal end of the collapsed bag portion of a 22F, 30 cc Foley bag catheter, and the silk end left long. Using a cystoscope, a No. 4 ureteral catheter was passed through the opening of the fistula located above the trigone and retrieved in the vagina by an assistant. The long heavy silk string was then firmly fixed, by several fine silk ties, to the urethral end of the ureteral catheter. The Foley catheter was then passed into the

Read on the Pan American Cruise Convention January 14, 1953
Accepted for publication May 6, 1952

[1] Young, H H Surg Gynec & Obst , **45:** 226, 1927

[2] Reich, W J and Wilkey, J L Urol & Cutan Rev , **47:** 160, 1943

[3] Miller, C O Urol & Cutan Rev , **53:** 83-85, 1949

[4] Fagerstrom, D P J Urol , **62:** 717-718, 1949

[5] Falk, H C and Bunkin, I A Surg , Gynec & Obst , **93:** 404-410, 1951

bladder and inflated with 25 cc fluid. Traction made upon the vaginal end of the string brought the area of repair (for denudation of the vaginal mucosa with high partial colpocleisis) nearer the vaginal outlet. With the aid of this modified Foley traction the procedure was immeasurably simplified.

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GRANULOMATOUS PROSTATITIS: A CONDITION WHICH CLINICALLY MAY BE CONFUSED WITH CARCINOMA OF PROSTATE

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This report was prompted by recent experience with a number of cases in which a preoperative diagnosis of carcinoma of the prostate gland was made but in which microscopic examination of tissue resulted in the diagnosis of granulomatous prostatitis.

Granulomatous prostatitis was first described as such in a study reported by Tanner and McDonald[1] in 1943. Little concerning its pathogenesis can be added to what is given in that report, in which the histologic appearance of this condition is described as that of chronic inflammation typified by the presence of many histiocytic cells. The normal structure of the prostate may be completely destroyed in some regions. The prostatic acini are replaced by dense infiltration of lymphocytes, plasma cells and large, pale-staining mononuclear cells; polymorphonuclear and eosinophilic leukocytes are also present. Foreign-body giant cells and pseudotubercles which appear to form around prostatic ducts are often present (fig. 1).

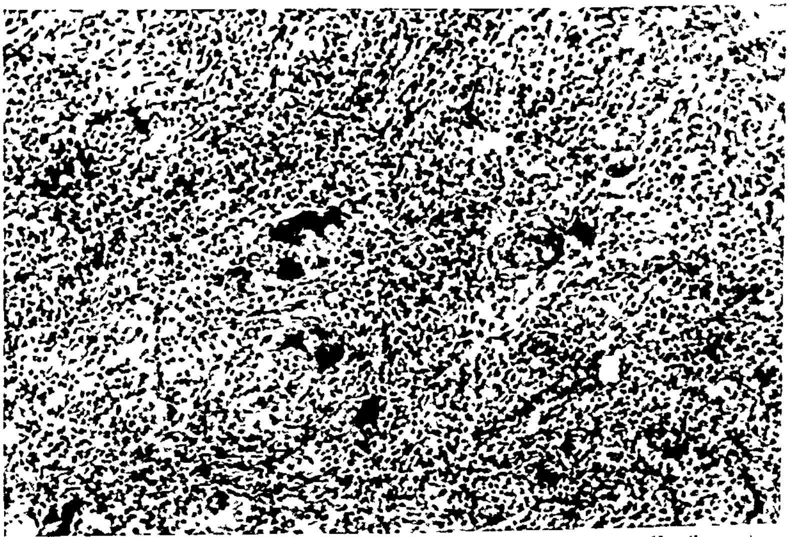

FIG. 1. Granulomatous prostatitis showing foreign-body giant cells (hematoxylin and eosin; × 125).

Read at annual meeting, American Urological Association, Atlantic City, N. J., June 26, 1952.

[1] Tanner, F. H. and McDonald, J. R.: Granulomatous prostatitis; histologic study of group of granulomatous lesions collected from prostate glands. Arch. Path., 36: 358–370, 1943.

Nesbit and Lynn[2] recently re-emphasized the confusion that may occur pathologically between tuberculous and granulomatous prostatitis.

We wished to clarify the confusion existing between prostatic carcinoma and granulomatous prostatitis, and to uncover symptoms and laboratory findings which might indicate the latter diagnosis preoperatively. Accordingly we obtained at random the records of 36 patients who had received the pathologic diagnosis of granulomatous prostatitis and who had undergone transurethral resections at the Mayo Clinic during the period from January 1943, to September 1949, inclusive. No attempt was made to study every case of granulomatous prostatitis in the records of the clinic and this report cannot be used as a basis for statistical analysis of the incidence of this entity.

In these 36 cases, the preoperative diagnosis of carcinoma of the prostate or probable carcinoma of the prostate had been made 20 times and benign hypertrophy 16 times. Granulomatous prostatitis is far less common than carcinoma of the prostate; thus the problem of its occurrence is not one of great magnitude. In any particular case, however, the finding of this condition may prove extremely interesting to the physician as well as gratifying to the apprehensive patient. Since certain of these cases have been striking and illustrate many of the features of the disease, it is felt that reports of a few representative cases will be enlightening.

REPORT OF CASES

Case 1.—A 65-year-old white man entered the clinic in August 1949, because of symptoms of urinary obstruction that began suddenly 3 weeks previously. He had been troubled by marked hesitancy, a small, dribbling stream, urination from 2 to 6 times nightly and some burning. Otherwise the history was noncontributory.

The only significant physical finding was a moderately enlarged prostate which, on rectal examination, felt as if it contained malignant tissue. Roentgenologic examination of the thorax disclosed that in the upper lobes of both lungs were fibrous and calcified lesions which were considered inactive. Determinations of the values for acid and alkaline phosphatase and for urea in the blood gave negative results. Routine laboratory studies of the blood, including a flocculation test for syphilis, gave negative results. Microscopic study of the urine showed no abnormalities and the volume of residual urine was only 10 cc.

During transurethral resection extensive contracture of the vesical neck was found. Twenty grams of tissue were removed and pathologic examination resulted in a diagnosis of granulomatous prostatitis (fig. 2). Convalescence was uneventful and the postoperative result was good.

Case 2.—A 61-year-old attorney entered the clinic in July 1949, with a history of obstipation, frequency, urgency and nocturia for 2 months. The patient had been told he had carcinoma of the prostate which presumably had extended beyond the prostatic capsule. Because of this presumed extension, radical perineal prostatectomy was not considered and transurethral resection had been advised. He was very apprehensive about the diagnosis of malignancy.

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[2] Nesbit, R. M. and Lynn, J. M.: Subtotal extirpation of the granulomatous prostate. J. Urol., 61: 766–774, 1949.

Results of physical examination at the clinic were negative except that the prostate was found to be moderately enlarged, firm and fixed; several pea-sized nodules projected from its surface. The examiner considered the prostate to be the seat of definitely malignant disease and the patient and his family were so advised.

Results of laboratory studies of the blood were within normal limits. Roentgenologic examination, including thoracic roentgenograms and excretory urograms, gave negative results except that a few prostatic calculi were found to be present. On catheterization 20 cc of residual urine were obtained. Urinalysis revealed the presence of pyuria; culture of the urine disclosed the presence of Escherichia coli. Microscopic examination of a specimen of prostatic secretion showed many pus cells; another specimen was reported to contain malignant cells.

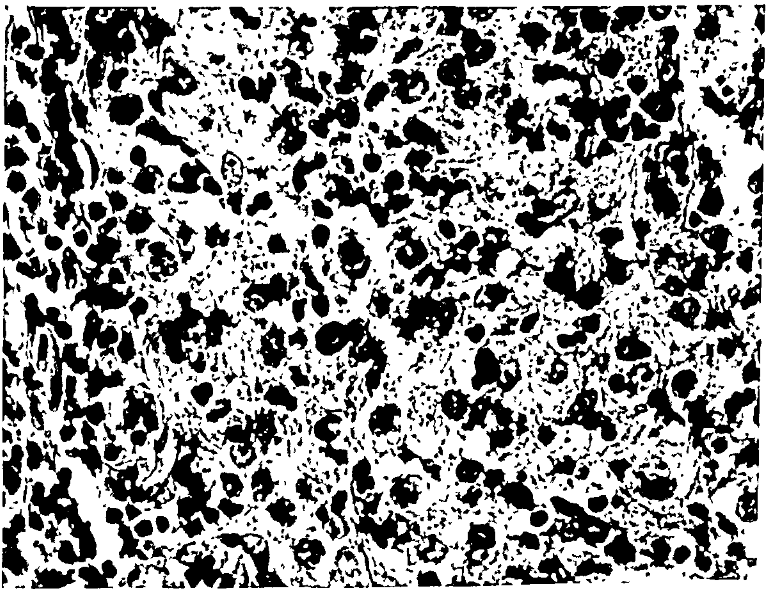

FIG. 2. (Case 1). Granulomatous prostatitis with lymphocytic infiltration, so-called plasma cell prostatitis. Note large mononuclear cells (*hematoxylin and eosin*; × 435).

When transurethral resection was performed, the median lobe was large but the hypertrophic tissue appeared to be benign. In the left lateral lobe was tissue which grossly appeared to be malignant. Thirty-three grams of tissue were removed during the operation and the immediate pathologic report was benign hyperplasia. Because of the nature of the case and especially because of the feeling of the surgeon that the tissue was carcinomatous, further study seemed indicated and it was decided that every piece of tissue would be sectioned and examined microscopically. As this study progressed, granulomatous prostatitis was evident in a number of portions but carcinoma could not be found.

Meanwhile, the patient made an uneventful recovery and was allowed to return home; stilbestrol was prescribed. When after 10 days, the continued microscopic study had failed to disclose carcinoma, administration of stilbestrol was discontinued. The patient returned for further examination in October 1949, at which time it was noted that the prostate was normal in size, smooth in contour and soft. None of the hard, irregular nodules remained.

The stained smears of prostatic secretions in which malignant cells had been reported were reviewed and the pathologist was of the opinion that cells previously considered malignant were undoubtedly large mononuclear cells of the nature shown in figure 2.

Case 3.—A 48-year-old white man entered the clinic in June 1947, for confirmation of the diagnosis of carcinoma of the prostate. This diagnosis, he said, had been made after he had undergone transurethral resection of the prostate for rather marked obstructive symptoms of short duration.

He made no particular complaints referable to the urinary tract when he arrived at the clinic. Pyuria was present and culture of the urine revealed the presence of Escherichia coli. There was no residual urine and values for acid and alkaline phosphatase in the blood were normal. Results of a roentgenogram of the thorax and an excretory urogram were negative.

Digital examination revealed that the prostate was small; the lateral lobes however were extremely firm and were considered to be definitely infiltrated by carcinoma. Cystoscopic examination disclosed a normal bladder; the prostate gland appeared to have been well resected but a few pieces of tissue were removed for examination. Microscopic study both of the slides sent from home and of those made from tissue removed at the clinic resulted in the diagnosis of granulomatous prostatitis.

Case 4.—A 49-year-old physician came to the clinic in October 1948, because his local urologist had found a hard region in his prostate and suspected malignancy. Six weeks previously the patient had experienced fever, chills and urinary frequency which had responded to chemotherapy.

Results of physical examination were negative except that a right direct inguinal hernia and a hard, fixed, nodular enlargement of the right lobe of the prostate were found.

Laboratory studies of the blood and urine disclosed nothing abnormal except a sedimentation rate for erythrocytes of 42 mm. during the first hour (Westergren). Roentgenologic examination of the thorax gave normal results, but a roentgenogram of the prostatic region revealed the presence of a few prostatic calculi. Because of the history of fever, chills and urinary frequency and because of the palpable consistency of the prostate, granulomatous prostatitis was suspected.

In order to establish the diagnosis it was deemed advisable to perform transurethral biopsy. Six grams of tissue were removed from the right lobe of the prostate which included the firm tissue palpated on rectal examination. A few tiny calculi were found. The pathologic report was granulomatous prostatitis. The patient has returned several times. He has reported no further trouble and the prostate has remained soft, smooth and entirely normal in consistency.

We discovered in 2 of the 36 cases of granulomatous prostatitis a histologic picture that has not been emphasized previously. Examination of tissue from both these patients disclosed tubercles (fig. 3) with central necrosis but with lack of the peripheral zone of lymphocytes regarded as typical of the histologic picture of tuberculosis. Extensive eosinophilic infiltration was noted throughout.

These 2 patients suffered from severe asthma and the eosinophilic reaction in the prostatic tissue was considered a manifestation of the systemic allergic state. A differential count of leukocytes was done on only 1 of the patients; this revealed eosinophilia of 50 per cent which could not be adequately explained. Carcinoma of the prostate was suspected in each of these cases both preoperatively and at transurethral resection because of the gross appearance of the tissue. Reports of these 2 cases follow.

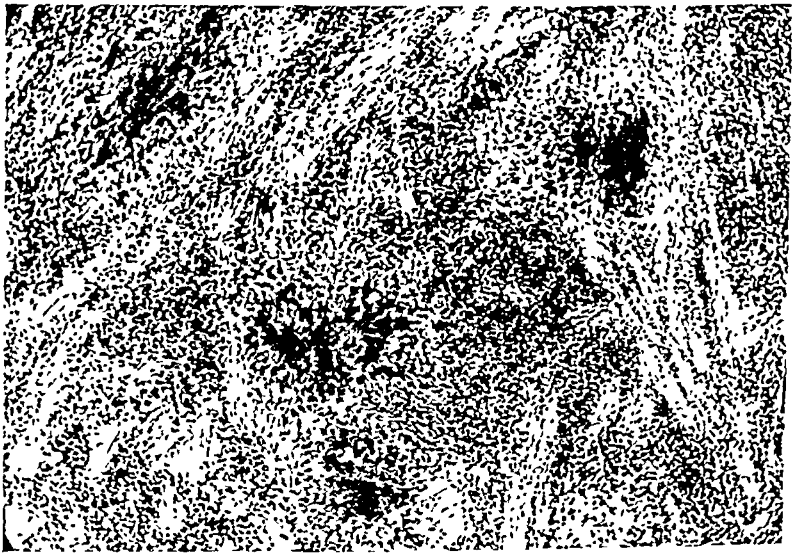

FIG. 3. (Case 6). Eosinophilic granulomatous prostatitis with formation of tubercles (hematoxylin and eosin; × 110).

Case 5.—A 46-year-old white man came to the clinic in September 1944, with complaints of chronic cough, wheezing and dyspnea subsequent to an infection in the upper part of the respiratory tract which had begun in February 1944 He also complained of urinary frequency and urgency with dysuria for one year. A diagnosis of asthmatic bronchitis had been made and response to therapy had been noted. Rectal examination at the clinic showed a moderately enlarged prostate gland that was firm in the left lobe; carcinoma was suspected.

Roentgenologic examination of the thorax and abdomen gave negative results. Laboratory studies of the urine and of the chemical constituents of the blood were within normal limits. Results of a flocculation test for syphilis were negative. Enumeration of leukocytes disclosed values ranging from 13,000 to 18,000 per cubic millimeter of blood. Differential counts of leukocytes showed an eosinophilia of 50 per cent. Studies of sputum for Mycobacterium tuberculosis failed to disclose its presence.

Cystoscopic examination of the anesthetized patient revealed an obstructive prostate and extensive trabeculation of the vesical musculature. Transurethral resection was performed and the operative diagnosis of carcinoma of the prostate was made. Twenty-seven grams of tissue were removed and microscopic study resulted in a diagnosis of granulomatous prostatitis with marked eosinophilic infiltration. There were numerous pseudotubercles with epithelioid cells radiating around necrotic centers. Evidence of extensive inflammation was present throughout the tissue and most of the cells were eosinophils. Convalescence was uneventful and the patient remained well except for asthma.

Case 6.—A 55-year-old white man was seen in August 1949, complaining of severe perineal pain and marked urgency and frequency of 3 weeks' duration. Tenesmus at the termination of urination was a prominent feature. It is significant to note that he was examined at the clinic in 1941 because of asthma and had been instructed in measures for its control. He had gotten along well from that standpoint until 10 weeks previously when he suffered a severe attack of asthma and it had been necessary to enter a hospital in his home locality. It was not until 7 weeks after the onset of this asthmatic attack that urinary symptoms had developed.

At the time of his admission to the clinic examination showed moderate enlargement of the prostate; the gland was hard and tender to light palpation. Catheterization disclosed 600 cc of residual urine. A review of the record at the time the patient was examined in 1941 revealed that nothing unusual about the prostate had been noted.

Transurethral prostatic resection was performed on August 22, 1949, with removal of 19 gm. of tissue which, on gross examination, revealed prostatitis and small patches of shotty induration. These indurated portions were 2 to 3 mm. in diameter and were extremely hard. They contrasted with the surrounding tissue which was softer and more resilient. Microscopic examination resulted in the diagnosis of granulomatous prostatitis (fig. 3) with eosinophilic infiltration.

Convalescence from the operation was uneventful. When the catheter was removed the patient voided with an excellent stream and had no residual urine. He was dismissed from our care.

Three months later the patient experienced an intense attack of asthma and also severe urticaria and facial edema. He was admitted to a hospital in another city and at that time anuria was present. Cystoscopic examination disclosed extensive edema of the vesical base; the ureters could not be catheterized. An artificial kidney was used for $4\frac{1}{2}$ hours. This produced considerable improvement in his condition, especially in reduction of edema. Cystoscopic examination 2 days later revealed great reduction in the degree of edema of the trigone and vesical base; catheterization of the ureters now was accomplished easily. Subsequent improvement was rapid and he was dismissed from the hospital.

The patient was seen again by the urologist in another city 2 months later. He had no urinary symptoms and was improved in health except for intermittent attacks of mild asthma and urticaria. These attacks continued and on April 12, 1950, following a severe asthmatic attack, he died at home of bronchopneumonia. Necropsy disclosed no significant findings except pneumonia.

Since this study was instituted, Melicow[3] described a patient in whom the pathologic findings are identical to those found in the 2 patients just described. He termed the condition "allergic granulomas of the prostate gland." His patient was treated by suprapubic prostatectomy; a gland weighing 14 gm. was enucleated and microscopic study of the tissue disclosed eosinophilic infiltration.

The extreme edema which was a prominent feature in case 6 of our series interposes another symptom which urologists must recognize when treating patients who exhibit allergic phenomena. It seems likely that in Melicow's case edema of considerable degree was present since he stated that examination, including a cystogram, revealed a "tremendously enlarged prostate gland," yet suprapubic prostatectomy resulted in the enucleation of only 14 gm. of tissue. Some of the enlargement probably was due to edema of the prostatic capsule and perhaps of the periprostatic tissues as well. The possible beneficial effect of antihistaminic drugs in cases of this kind must be considered.

COMMENT

Study of the histories in these 36 cases fails to reveal any feature which is specific for granulomatous prostatitis. History of recent fever or febrile episodes immediately preceding the onset of urinary symptoms might be of some value in aiding the physician to avoid an erroneous diagnosis of carcinoma based on palpation of a firm, irregular prostate. Of course, infection can develop in cases of prostatic carcinoma, especially after catheterization. However, it is unusual for a patient with prostatic carcinoma to undergo repeated febrile episodes accompanied by urinary frequency, urgency and tenesmus. This group of symptoms should place the physician on guard against making a diagnosis of carcinoma when he finds a hard, firm, irregular prostate. Careful microscopic study of tissue obtained for biopsy by transurethral or perineal routes establishes the diagnosis.

Pyuria, grade 2 or more (based on scale of 1 to 4), is a common finding, occurring in 57 per cent of cases of granulomatous prostatitis included in this study. This incidence is probably more than might be expected in a like number of cases of benign hypertrophy or of carcinoma of the prostate. No single species of organism appeared frequently when the urine was cultured. Most of the usual bacterial offenders encountered in urinary infections were met with in this study.

Only 2 patients had significant anemia and none gave a history from which one might suspect recent infection with a virus. Three patients displayed old calcified apical lesions of the lung but in none of these was there anything to suggest genitourinary tuberculosis. In 2 of these 3 patients the prostate felt as if it might be carcinomatous. Tanner and McDonald[1] demonstrated adequately that granulomatous prostatitis is not tuberculous in origin. Determinations of values for acid phosphatase were done in 12 of the cases that were considered clinically to be carcinoma of the prostate; all values were within normal limits. None of the roentgenograms showed evidence of metastasis.

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[3] Melicow, M. M.: Allergic granulomas of the prostate gland. J. Urol., 65: 288-296, 1951.

RESULTS OF TRANSURETHRAL RESECTION

The results were divided into three categories; in 28 cases these were classified as good, in 3 fair and in 5 poor. Analysis of the group in which results were poor seems indicated. One case of the group with fair results and 2 of the group with poor results included patients who had neurogenic vesical dysfunction. One patient with poor results had interstitial cystitis and cicatricial posterior urethritis and had undergone transurethral resection elsewhere. Another patient in this group had a huge atonic bladder with a large diverticulum, and the fifth patient with poor results died of anuria 9 days after operation. Necropsy in this last case disclosed the presence of an extremely small adenocarcinoma, grade 2, in the periphery of the prostate, a so-called occult carcinoma.

None of the patients in our series and none of those reported previously by Tanner and McDonald[1] are known to have had carcinoma of the prostate after leaving the clinic. There is no reason why they should not experience carcinoma in later years just as anyone with a previously benign prostate might; whether or not the patient with the occult carcinoma would later have noted clinical symptoms from it is purely a matter for speculation. In our opinion there is no relationship between granulomatous prostatitis and carcinoma of the prostate.

The amount of tissue removed in these cases by transurethral resection averaged 22 gm.; the largest amount was 73 gm. and the smallest was 5 gm.

It is interesting to note in the majority of cases how positive the examining physicians were about the presence of malignant disease based on digital examination of the prostate gland. Notes made in the history concerning examinations at the clinic by senior clinicians and experienced urologists included such expressions as "unquestionably malignant," "positively a cancer of the prostate" and "beyond any doubt a malignant gland." Such expressions of opinion serve to emphasize the importance of caution when offering preoperative advice.

What type of treatment might these patients have received if a presumptive diagnosis of malignancy had been made and therapy instituted without microscopic confirmation of the diagnosis? Castration or intensive use of stilbestrol or other hormonal drugs might well have been advised. Lack of evidence of metastasis to bone and the presence of normal values for serum acid phosphatase should deter the urologist from making this error. It certainly would be unwarranted to castrate a man for so benign a lesion as granulomatous prostatitis. Castration should not be done without proof of the presence of carcinoma either by microscopic examination of tissue or by roentgenologic evidence of metastasis to bone. Radical perineal prostatectomy should not be advised on the basis of finding a hard nodule in the prostate. In this situation, also, positive confirmation of the diagnosis by examination of tissue should be required.

SUMMARY AND CONCLUSIONS

Of a total of 36 patients with granulomatous prostatitis, 20 patients were considered to have carcinoma of the prostate as evidenced by preoperative digital examination of the gland.

Reports are presented of 6 cases which illustrate various phases of granulomatous prostatitis. These include the cases of 2 patients who had eosinophilic granulomatous prostatitis.

This study reveals nothing in the history or physical findings which can be used as positive evidence to differentiate between malignant disease and granulomatous prostatitis. It seems likely that this condition occurs more often than is recognized and that some patients with this benign condition are in danger of being treated for carcinoma of the prostate.

The use of hormonal therapy, such as the administration of stilbestrol, and especially the use of surgical castration, must not be considered in the absence of a positive biopsy or in the absence of roentgenologic evidence of carcinoma of the prostate. Granulomatous prostatitis can produce a consistency of the prostate identical to that produced by carcinoma and, unless tissue is examined microscopically, the proper differential diagnosis cannot be established.

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NOTES ON PROSTATIC SURGERY, AND THE RESULTS WHICH SHOULD BE EXPECTED OF IT

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Prostatic surgery began about the same time as human flight in aeroplanes, and has been marked by a similar steady, rapid and, indeed, spectacular progress.

In its early days, prostatic surgery was very deadly. The reasons for this were manifold, and it is interesting today to see how the various causes of death have been cut down and eventually for the most part eliminated. Fifty years ago operations were performed only in desperate, far advanced cases, little or nothing was known about the effects of prostatic obstruction on kidney function, and there were only poor and inadequate means of dealing with ever-present infection and with postoperative hemorrhage. Lastly, the treatment of many intercurrent and complicating conditions, such as diabetes and cardiovascular disease, was much poorer 50 years ago than it is today.

In considering our present position, the most fundamental question is "what is the object of prostatic surgery?" One must answer that there are in the main, and omitting such infrequent conditions as abscess of the prostate and injury to the prostate, only two primary objects of prostatic surgery; namely, 1) to relieve prostatic urinary obstruction, and 2) to cure early cancer of the prostate. Secondary objects of great importance are to avoid postoperative complications and to prevent fatalities. Each urologist should keep these objects clearly in mind at all times, and never allow himself to be diverted by enthusiasm for any particular method of operating.

Everyone knows that prostatic surgery becomes better and safer each year. It is well to stop and think why this is so. There are a number of reasons, roughly as follows:

1) Better pre- and postoperative care, with attention to fluid balance, electrolyte balance, nutrition, vitamin intake, and the giving of parenteral fluid, blood and plasma. It is hard to exaggerate the importance of this group of improvements.

2) Better methods for the treatment of intercurrent diseases, such as cardiovascular disease and diabetes.

3) Early ambulation, the use of anticoagulants and other methods for the prevention of thrombosis.

4) Better methods for the control of early and late postoperative hemorrhage. It should never any longer be necessary to open the bladder to arrest hemorrhage, as it can all be done instrumentally.

5) Better nursing care. The former reluctance of female nurses to care for urologic cases has been replaced by enthusiastic interest and technical competence.

Read at annual meeting, American Urological Association, Atlantic City, N. J., June 26, 1952.

6) The organization of resident staffs, which ensures competent care at all hours of the day and night, and prompt attention to emergencies.

7) The effective treatment and prevention of alkaline wound infections. This has proved to be very simple. Nothing is necessary but continuous irrigation with weak acid solution.

8) The antibiotic drugs, which have practically eliminated the former *bete noir* of urologists, ascending renal infection or urosepsis.

9) Patients come in earlier for operation, so that there are fewer of the terribly bad risks.

Please note that these nine reasons do *not* include "improved methods of operation."

One point deserves special mention. Recently there have appeared a few advocates of immediate operation in cases with impaired renal function, provided no serious infection is present. Most cases so handled undoubtedly will survive, but this practice involves a certain added risk, which I think is neither necessary nor justified. Renal impairment due to urinary obstruction depends upon decompensation of the ureters, that is, they can no longer conduct urine from the kidneys to the bladder in the normal way, nor under the normal pressure conditions. If such decompensation continues very long, the ureters become dilated and thoroughly incompetent, so that they afford an easy path for infection to follow to the kidneys. In such cases renal functional tests may return to normal very quickly after tube drainage by catheter or by suprapubic tube is begun, but it takes a much longer time for the ureteral dilatation to disappear and for normal peristalsis to be re-established. It is better and safer to wait until this time before operating upon the prostate, whether it be a week or several months. The state of the ureters can usually be ascertained by excretory urography. While this conservative procedure may save only an occasional patient, the mortality of prostatic surgery is now so low that no urological surgeon can afford to take even the remotest chance of an unnecessary fatality.

It is obvious that all the recognized methods of operating upon the prostate are good methods, and will produce good results in competent hands. It is no longer necessary to labor this point. Since each operative method is said to have, and undoubtedly has, certain advantages, it is absolutely essential that those who pretend to train young urologists instruct them adequately in the performance of operations by all the known methods, so that they will be able to choose freely the operation best suited to each case, and not be influenced by prejudice in favor of any certain method, or by any feeling of inadequacy in respect to any certain method. Only in this way can urology as a specialty escape the charge of an unscientific particularism.

The matter of radical operation for early carcinoma is a very important one, and is attracting a rising tide of interest. Only if urologists generally advocate and push the method at every opportunity, and instruct the profession generally in the way to discover suspicious cases by routine digital rectal examination, can we hope to make real progress. The operation, it has already been shown, will give good results in better than 50 per cent of cases; it is only necessary to have more early diagnoses. Attention is drawn to the advantages of the perineal route for performing the radical operation and for obtaining material for frozen section.

There should be a word of caution about the pathological diagnosis. The metaplasia occurring around infarcts of the prostate, as well as other changes seen in hyperplastic or chronically inflamed prostates, or those which have been subjected to radiation or to electrocoagulation may give rise to pictures easily mistaken for carcinoma. The microscopic diagnosis should be undertaken only by those trained and thoroughly competent in this particular field.

In considering the success and safety of prostatic surgery, we must keep in mind the number of the patients who seek relief, but die before any operation can be performed on the prostate gland. In 1919, Galbraith of Glasgow reported this figure at 20 per cent. In the years 1936 and 1937, at the Jefferson Hospital, in Philadelphia, on my own service, 22 per cent of the ward patients admitted for prostatic obstruction died before the prostate could be operated upon, and in spite of our best endeavors. Patients in this class are seldom referred to in articles on prostatic surgery, and yet their deaths are just as tragic as those subsequent to operations on the prostate. However, it must be obvious that the number of patients failing to reach the operating table is at the present time nothing like 20 or 22 per cent of the whole. Actually a revolution in this respect has gone on right under our noses and we are only beginning to wake up to it. In a consecutive series of 450 of my own patients, only a single one has not had an operation on his prostate, and he is alive and in good condition with urinary drainage through a suprapubic tube which he apparently does not wish to get rid of as he will not return for further operation. This is a preoperative mortality of zero. The preoperative mortality on the ward service is greatly reduced, but unfortunately lack of time and of assistance have prevented me from ascertaining the exact figures.

This desirable state of affairs is due obviously to two reasons: First, the number of very advanced cases, with severe renal damage and poor general condition is greatly reduced owing to the increased willingness of physicians to recommend early operation, and the increased willingness of patients to accept that advice. This change of attitude is due to the better results of surgery, so that we have here a beneficent circle which will no doubt go on improving matters more and more. Second, the chances of salvaging the bad risks have been increased in spectacular fashion by the antibiotic drugs. It seems likely that these drugs have done much more good, proportionately, in this field than they have in saving lives in the postoperative period. While the postoperative mortality in the hands of the best operators has been really good for more than a quarter of a century, we can now say, and we should never cease to affirm it energetically, that practically every person suffering from prostatic obstruction, whether he be good risk, indifferent risk, or bad risk, can now be brought successfully through an operation.

What, then, should the mortality be in prostatic surgery? This is a matter of great interest and also, it seems to me, an area of great confusion. I believe that it would be well, at this point in the history of medical progress and in the development of urology, to examine this subject very critically, and establish some standard which all could recognize, and which every urologist would have to meet in order to be regarded as competent in this branch of his work.

In the beginning only the most desperate cases were operated upon, and the mortality rate, judged from the statements of those surgeons who lived through that era, was surely not far from 50 per cent. The drop in the mortality rate has been continuous, and spectacular, yet the old notion that prostatic surgery was dangerous has persisted in many quarters. It still makes a good many patients fearful, and it still makes a good many doctors hesitate about recommending surgery. Furthermore, and sad to say, it still affects some urologists so that they are satisfied with mortality rates which are too high.

How high should the mortality rate be as of today? The work of Hugh Young did perhaps as much as anything to clarify the situation in the previous generation. His global operative mortality for 1049 cases of perineal prostatectomy from 1902 to 1922 was 3.4 per cent. However, there was a series of 128 consecutive operations in 1906, 1907 and 1908 without fatality, and another similar series of 198 cases running from 1919 to 1922. In the years from 1917 to 1922 inclusive he operated upon 234 patients with one death, a mortality of 0.43 per cent. All this was before the days of antibiotics, and can be ascribed only to painstaking, competent work before, during and after the operation. E. G. Davis of Omaha has reported a series of 139 perineal prostatectomies without fatality. B. A. Thomas of Philadelphia is said to have reported 100 consecutive suprapubic prostatectomies without fatality in 1922.

Creevy* has studied the subject, and quotes Nesbit with a rate of 1.81 per cent in 2425 transurethral resections, Thompson of the Mayo Clinic with a rate of 1.2 per cent in 11,522 transurethral resections, and himself with a rate of 0.6 per cent in 1000 transurethral resections. Darget of Paris and Bordeaux joins this select group with a series of 180 transurethral resections with a mortality rate of 0.6 per cent.

Creevy further tabulates a great number of domestic and foreign surgeons with rates varying from 1 to 39 per cent for suprapubic prostatectomy and from 0 (in a series of 65 operations) to 15 per cent for retropubic prostatectomy. All of these reports were made in the years 1945 to 1949. Terence Millin's own record for 757 cases of retropubic prostatectomy was, in 1949, 4.5 per cent. At the 1949 meeting of the International Urological Society in Barcelona 10 surgeons reported their results. Serralach of Barcelona had 150 consecutive perineal prostatectomies without a death. The others had rates varying from 0.6 per cent to 18.15 per cent. Perhaps the best series of 100 or more retropubic operations to date is that of Thomas Moore of Memphis, whose rate is 1.7 per cent. Latchem and Emmett report 345 transurethral resections in patients over 80 years old with mortality of 2.6 per cent.

I wish to contribute to this subject a personal series of 502 consecutive operations on 449 patients without any operative mortality whatever. This indicates

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* J. Urol., **65:** 876–882, 1951.

10.6 per cent of repeat operations, apparently a normal figure. The ages of these patients were from 18 to 93, with 98 over 70 years old, 16 over 80 years old, and 2 over 90 years old. The great majority lay, as usual, in the sixth and seventh decades of life. Of these operations, 378 were transurethral resections, 103 were perineal prostatectomies, 13 were radical perineal prostatovesiculectomies for early carcinoma of the prostate, and one was a retropubic prostatectomy. In 127 instances preliminary bladder drainage for various lengths of time was used, 114 by retention catheter, 13 by suprapubic tube. In 374 instances there was no preliminary bladder drainage. Benign prostatic hypertrophy was present in the tissue removed 388 times, carcinoma of the prostate 31 times, and contracture of the vesical orifice 29 times. Other complicating lesions were present in a number of cases, as for example 13 instances of stricture of the ureter, 13 of renal and ureteral calculi, 12 of bladder neoplasm, 9 of diverticulum of the bladder, 9 of vesical calculus, etc. Postoperative complications were minimal. Bleeding occurred 29 times, all arrested without performing cystotomy, epididymitis 21 times, pulmonary complications 5 times, recto-urethral fistula once. This fistula opened 7 days after perineal prostatectomy. Suprapubic cystostomy and sigmoid colostomy were instituted at once. Four months later the fistula was closed by the Young-Stone operation and the suprapubic tube removed. One month later the colostomy was closed. The ultimate result was excellent. Poor urinary control was a feature in only three cases. One of these was a contracted bladder which gave rise to intractable frequency and urgency. There were no instances of urosepsis, postoperative hernia, or osteitis pubis, and only 2 cases which were thought to be mild instances of hemolytic lower nephron nephrosis.

Of the 377 transurethral resections, 67.6 per cent left the hospital in 10 days or less, 77 per cent in 14 days or less, and 85.6 per cent in 19 days or less. Only 10 cases remained more than 30 days. Of the perineal prostatectomies, 28.15 per cent left the hospital in 14 days or less, 71.84 per cent in 21 days or less, and 91.26 per cent in 29 days or less. The maximum hospital stay was 64 days. The 7 cases of suprapubic prostatectomy were discharged in from 8 to 21 days. Of the radical perineal prostatectomies, 1 case left the hospital in 7 days, 84.6 per cent in 21 days or less and 100 per cent in 38 days or less.

I believe that the facts and figures here presented show that at this time and in this country no one performing prostatic surgery should any longer dare to regard a mortality rate of 4 or 5 per cent with equanimity, but that on the contrary every urological surgeon should strive to have his mortality rate well under 1 per cent, with the feeling that if it rises much above this figure some details of the treatment are being neglected or incorrectly handled. Every fatality must be most carefully studied to see if it was not in some way preventable; in other words the target mortality is now zero. I believe firmly that each one of us should single-mindedly analyze his results, selecting his technical methods to obtain the best results, and for no other reason whatever.

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SPINDLE CELL SARCOMA OF THE PROSTATE GLAND: CASE REPORT

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Sarcoma of the prostate gland in adults is a rare disease and as far as we have been able to determine, approximately 225 cases have been reported in the medical literature; therefore every case should be reported.

Sarcoma of the prostate may occur at any age, but is most frequently found in the first decade of life. Its etiology is obscure. The simplest pathological classification is that given by Stevens and Barringer and is based on tissue origin. According to these authors, sarcoma of the prostate may be divided into two major groups: a) The primary group includes the rhabdomyosarcomas, lymphosarcomas and a subgroup in which are classified the spindle cell sarcoma, fibrosarcoma, myxosarcoma, round cell sarcoma and the giant cell sarcoma; b) the second group includes the anaplastic carcinoma actually resembling the lymphosarcoma.

The symptoms of sarcoma of prostate are those of vesical neck obstruction. Pain occurs frequently. The physical findings on examination are not characteristic. Usually the prostate feels uniform, smooth, tense, symmetrical and nontender. Such tumors should be differentiated from abscesses, hypertrophy, tuberculosis, carcinoma and cysts of the prostate, as well as from cysts of the seminal vesicles. Metastases are regional in 76 per cent of the cases (Lowsley). Distant metastases occur in half of the cases.

Prognosis is poor. Average duration of the disease is 9 months. Very little can be accomplished by treatment. Deep x-ray therapy and/or radium therapy with surgical relief of the urinary retention is the only treatment which can be offered.

CASE REPORT

R. W. (Hosp. No. 50-2036), a 68 year old man, came to the hospital on March 16, 1950, with the chief complaint of difficulty of urination. The present illness had started 1 year prior to his admission, when frequency of urination, mild dysuria, slowing of the urinary stream, some hesitancy and urgency gradually developed. No history of hematuria, backache, renal colic or loss of weight was obtainable.

Past history, family history and systemic inquiry were noncontributory.

On physical examination the patient appeared comfortable and well nourished. On rectal examination, the prostate was found to be three times normal size, smooth, globular, movable and not tender. The median sulcus and lateral margins were well defined. The residual urine measurement was 480 cc.

Physical examination otherwise was within normal limits.

Our tentative diagnosis on admission was benign prostatic hypertrophy. Gross examination of the urine showed some cloudiness and microscopy revealed many

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bacteria and white blood cells. Sedimentation rate was 42 mm. per hour. The blood count and differential were normal. Blood nonprotein nitrogen was 46 mg. per cent, urea nitrogen 14.7 mg. per cent, creatinine 2.0 mg. per cent. Alkaline phosphatase was 3.5 Armstrong units, and acid phosphatase 3.9 Armstrong units.

Excretory urography revealed an elevation of the floor of the bladder suggestive of prostatic hypertrophy, and otherwise was normal. Electrocardiograms and chest films were reported normal.

On March 22, 1950, on the fourth hospital day, cystoscopy was performed. Examination of the prostate showed a moderately large subtrigonal middle lobe, a small left lobe and moderately enlarged right lateral lobe. Rectal examination over the inlying catheter revealed a hard nodule incorporated in the right lateral lobe, nearer to the rectum than to the urethra. The consistency of this nodule suggested nodular glandular hyperplasia.

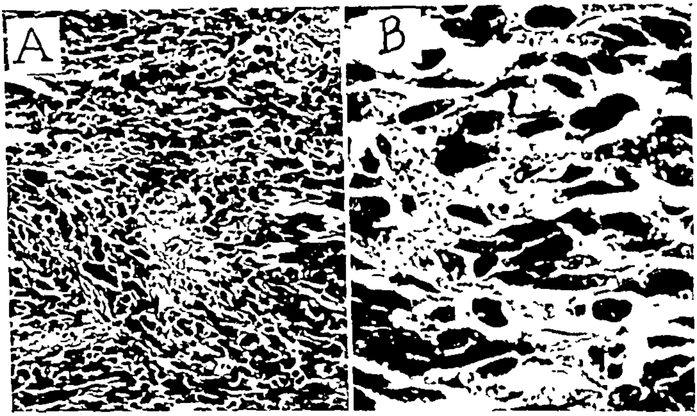

Fig. 1. *A*, bundles of sarcoma replacing prostate gland. *B*, high power view of spindle cell sarcoma revealing large oval and spindle cells with large hyperchromatic and vesicular nuclei.

The following day a bilateral partial vasectomy and a suprapubic prostatectomy were performed. During the removal of the prostate, no satisfactory line of cleavage could be found between the gland and its capsule. The prostate felt hard and fibrotic. During the operation it became evident that we were dealing with a malignant condition. The specimen weighed 29.5 gm. Microscopic examination of the tissue revealed that the prostatic gland was replaced by tumor consisting of bundles and solid masses of large oval and spindle cells showing large hyperchromatic and vesicular nuclei (fig. 1). In many areas, masses of tumor cells were seen within vascular channels. The pathological diagnosis was spindle cell sarcoma of the prostate gland.

The patient had an uneventful postoperative recovery. He received a full course of x-ray therapy to the abdomen and pelvis. A bilateral intracapsular orchiectomy was performed on the seventh postoperative day on an experimental basis. The patient was discharged on the thirty-eighth hospital day, the suprapubic wound well healed and voiding satisfactorily.

Radiography of the chest on August 3, 1950 was negative.

On August 23, 1950, five months following the suprapubic prostatectomy, the patient was re-admitted because of acute urinary retention and loss of approximately 10 pounds of weight. He looked pale and exhausted and complained of severe suprapubic pain. Rectally a hard nodular mass was felt in the prostatic area, with definite involvement of the lateral pelvic walls. The laboratory studies were the same as on the first admission, except for moderate anemia.

An emergency permanent suprapubic cystostomy was performed and the patient left the hospital 12 days later. During this admission the patient complained consistently of pain felt along the posterior aspect of both his thighs, and it was necessary to give 21 mg. pantopon three times daily.

The patient's final admission was on October 2, 1950 because of bleeding from the suprapubic wound through the inlying catheter.

The blood studies revealed the following: Red blood cell count 3,020,000; hemoglobin, 9.0 gm. per cent; nonprotein nitrogen, 44.5 mg. per cent; blood urea nitrogen, 27 mg. per cent; creatinine 2.35 mg. per cent; alkaline phosphatase, elevated to 11.6 Armstrong units, and the acid phosphatase, 2.7 Armstrong units.

During this third admission the patient received an additional course of x-ray therapy for hemostatic purposes. He complained of intense pain in both extremities and pain in the left half of the chest, pleuritic in character. His condition grew worse and he expired on October 27, 1950, seven months and 4 days after his initial operation.

An autopsy showed 500 cc bloody exudate in the peritoneal cavity. The bladder was contracted, hard, indurated and showed invasion by metastatic nodules on microscopic studies.

Metastatic nodules were also found in the liver, small bowel, colon, mediastinal lymph nodes, the visceral pleura, in six different ribs and in the seventh thoracic vertebra, in the capsule of the spleen and in the right adrenal gland.

SUMMARY AND CONCLUSIONS

A case of spindle cell sarcoma of the prostate occurring in a 68 year old man is presented. The patient was treated with a suprapubic prostatic enucleation before the diagnosis was made. He received deep x-ray therapy and had a bilateral intracapsular orchiectomy. He expired 7 months and 4 days after the diagnosis of a spindle cell sarcoma of the prostate gland was established. Autopsy findings are reported.

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AN UNUSUAL CASE OF PENILE CARCINOMA

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Carcinoma of the penis, though not uncommon, is a relatively infrequent lesion in the United States. Approximately 2.5 per cent of all carcinomas in the males of this country are found on the penis. A slightly lower incidence exists in England, while that for Europe as a whole is about 5 per cent. Carcinoma of the penis reaches its highest incidence in certain Asiatic countries: Siam, Tonkin, Java, 19 per cent; China 18 per cent; non-Moslem India, 10 per cent.[1] It is relatively infrequent among the Mohammedans of India and in the other Moslem nations. Dean has reported the only case of penile carcinoma in a Jewish male, and this had its origin in the scar of a previously cauterized luetic lesion.[2]

However infrequent the lesion, the subject of carcinoma of the penis has been adequately covered and reviewed many times in medical literature and from all viewpoints, etiology,[3] racial immunity,[4] the prophylaxis of circumcision,[5] carcinogenicity of smegma,[6] significance of pre-existing lues,[7] methods of therapy.[8, 9, 10] It would be redundant to repeat such an accounting. However, since there has been only one reported case of carcinoma of the penis in a circumcized Jewish male, we believe that the report of a second case would be of interest.

CASE REPORT

A 73 year old Jewish male had undergone a ritual circumcision on the eighth day after birth. He was first seen in the Tumor Clinic of Michael Reese Hospital on December 5, 1951, eighteen months after the onset of his disease. The lesion had its origin as a small red papule on the shaft of the penis, near the glans. It gradually ulcerated and increased in size until it involved the entire dorsum and lateral surfaces of the shaft of the penis. All this time the patient had been under care of several dermatologists who had made a variety of diagnoses and had instituted a variety of therapeutics. The lesion had been considered a dermatitis venenata, an eczematoid dermatitis, a chronic granuloma.

Physical examination revealed an extensive, red, weeping, crusted lesion on the dorsum of the penis measuring 3 by 4 cm. (fig. 1, *A* and *B*). The lesion appeared

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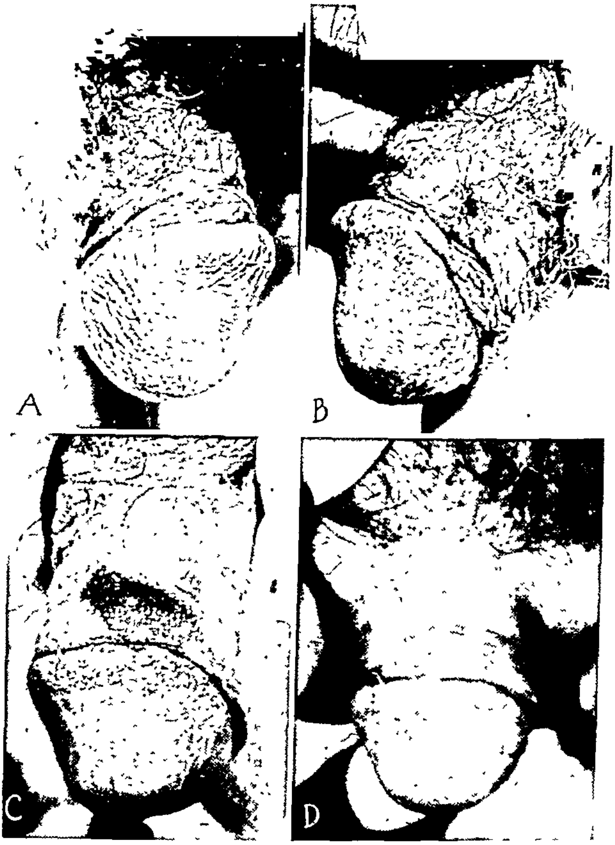

FIG. 1

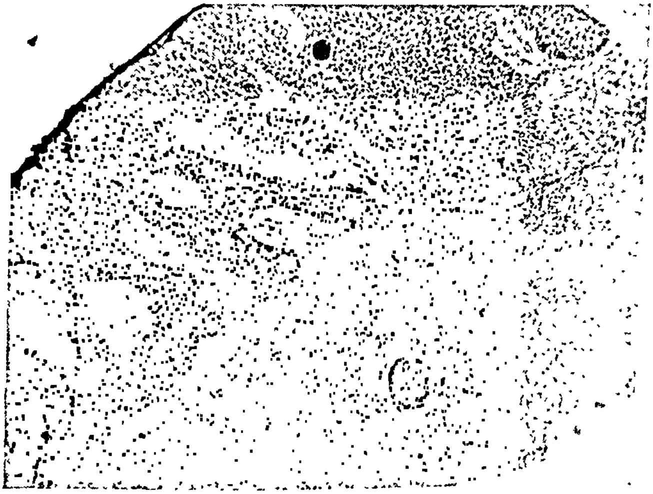

FIG. 2

to be superficial and there was no induration of its edges or of the underlying tissues. The patient complained of severe itching and pain in the involved area. There was no evidence of regional lymphadenopathy. Because of the progressive nature of the lesion and its failure to respond to the previously administered medications such as boric acid soaks, calomine lotion, zinc oxide, aqua calcis, tyrothricin, we suspected malignancy and a biopsy was taken.

Microscopic sections showed a markedly thickened squamous epithelium covering a vascularized fibrous tissue densely infiltrated with round cells. The epithelial cells differed markedly in size and were in disorderly arrangement within the epidermis. Mitotic figures were present in the corneum and basalis stratum. Basal cells penetrated the underlying tissues in several foci. The microscopic diagnosis was squamous cell carcinoma (figs. 2 and 3).

Radium was chosen as the therapy of choice because of the extreme superficial nature of the lesion. Amputation was deemed too drastic for such a locally limited lesion as described. A special radium mold was constructed to adequately cover the involved area and a margin of 1 cm. around all borders. The radium content of the plaque was 100 mg., consisting of twenty 5-mg. tubes of radium distributed uniformly over the convex surface of the mold made to fit the dorsum and lateral surfaces of the penile shaft. A dose of 3000 mgh, equivalent to 6000 gamma roentgen, was administered to the base of the lesion in seven treatments over a period of 8 days, from December 10 through December 17, 1951. The treatment periods to achieve such a dose were 3–5 hours daily. A uniform radiation reaction appeared within 2 weeks, covering the whole dorsum with a moist epidermite. This regressed gradually until on January 29, 1952, the lesion was 90 per cent healed, and only a small area of residual epidermite remained (fig. 1, *C*). By February 19, 1952, two months after the treatment had been completed, the radiation reaction had completely subsided and the lesion healed (fig. 1, *D*). The patient was asymptomatic. The patient remained free of disease when last seen December 1952.

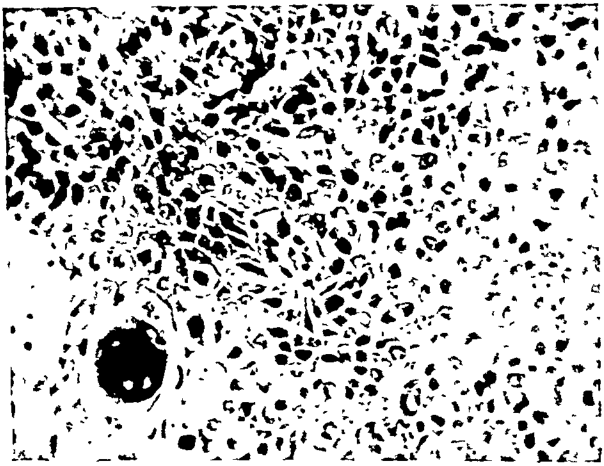

FIG. 3

In summary, an unusual case of penile carcinoma has been presented. The lesion is of interest since it is doubly rare, occurring as it did, localized to the shaft of the penis, of a circumcized Jewish male.

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CANCER OF PENIS: A REPORT OF EIGHTY-EIGHT CASES

JOHN H. FURLONG, JR. AND CHARLES A. W. UHLE

The purpose of the paper is to add to the knowledge of the course of cancer of the penis by reporting an unselected series of 88 cases in which the diagnosis was made more than 5 years ago. Of the entire group, regardless of the original status of the disease or the type of treatment given, 60 patients eventually died with or of tumor or its treatment, seventeen died of causes unrelated to tumor or with the status of the tumor unknown, and eleven lived at least 5 years after treatment and were apparently cured. The material comes from the Urology Section of the Radiology Department of the Philadelphia General Hospital and includes all cases of proven cancer of the penis seen there between the years 1921 and 1946. Approximately twenty additional charts were reviewed but found to be incomplete for analysis.

No factors of etiologic significance were found other than that specific mention of phimosis or the presence of a prepuce was made 53 times. There were no patients of Hebrew faith among the fifty-three in which religion was mentioned Fifty-eight were Caucasian; twenty-nine, Negro; and one was Chinese.

The age at which diagnosis was made ranged from thirty to ninety-one and averaged sixty. The number of cases occurring in each ten year age group is shown in table 1. It is seen that the peak incidence was between the ages fifty-one and eighty.

HISTORY

A definite penile lesion was noted at some time by all but 3 patients able to give a history, and in those 3 patients a small lesion had been concealed by a phimosis. All the complaints were directly referable to rather obvious local or systemic effects of the primary or metastatic disease. Of interest is that the chief complaint of 4 patients was nonhealing of an apparently routine circumcision. A history of a chancre or antiluetic treatment was noted 11 times and positive blood serologic tests were found in an additional 18 cases for a total of twenty-nine (or 33 per cent) luetics.

Patient delay in seeking medical advice was notable in that among 75 patients from whom this information was obtained, twenty (26.6 per cent) deferred examination for over one year (table 2). One of the patients who delayed 4 months in seeking treatment received cautery destruction of a growth on the glans two times by his private physician. He disappeared 6 years and when seen then had a moderate sized grade 2 squamous cell carcinomatous ulcer of the glans. In the entire series of 88 patients, fifteen of the patients (17 per cent) first presented themselves for diagnosis when all or part of the penis had sloughed off. Physicians' error in diagnosis occurred with 10 patients and thereby caused delay in treatment for an average of 11 months. Obviously, immediate biopsy is demanded of all chronic darkfield negative penile lesions.

Read at annual meeting, Mid-Atlantic Section, American Urological Association, Philadelphia, Pa. April 19, 1952.

PHYSICAL EXAMINATION

On physical examination, a tumor was noted on the glans alone 17 times, on the prepuce alone 10 times, and on the shaft alone 8 times. The latter group includes one sarcoma and one malignant melanoma. All three regions or two of the three were involved with tumor growth 30 times, and in fifteen others all or part of the penis had sloughed off. No specific location was named as the site of the tumor in the remaining 8 cases. Also at physical examination, progression of the lesion was found to have caused urinary fistulae six times and acute urinary retention 3 times. The presence of inguinal adenopathy was noted in 58 cases (66 per cent), whereas specific mention of the absence of inguinal adenopathy occurred only 8 times. Inguinal nodes were examined microscopically in twenty-seven of the 88 cases and twenty (23 per cent) showed metastases. The actual incidence of node metastases must have been appreciably higher than 23 per cent since several advanced cases with inguinal node ulceration were not subjected to biopsy.

TABLE 1

AGE	CASES
21-30	3
31-40	9
41-50	10
51-60	21
61-70	20
71-80	19
81-90	5
91	1

TABLE 2. *Delay in diagnosis in 75 cases*

TIME FROM FIRST SYMPTOM TO FIRST VISIT TO PHYSICIAN	CASES
1 to 3 months	25 (33.3%)
3 to 6 months	16 (21.3%)
6 to 12 months	14 (18.6%)
Over one year	20 (26.6%)

PATHOLOGY

Biopsy reports were available in all but 5 cases. Among these 5 cases, two had had partial penectomy elsewhere, and in all the clinical extent and destructiveness of the lesion could be accounted for only by carcinoma. Seventy-nine cases were classified as squamous cell carcinoma; in 2 cases there were areas of both squamous and basal cell carcinoma. There was one case each of sarcoma and malignant melanoma.

Forty-two of the tumors were graded according to the method of Broders (table 3). As has been noted in other reported series, grades 1 and 2 lesions greatly predominate.

TREATMENT

The types of treatment given have been separated into two groups; those in which the object was purely palliation, and those performed with some chance of cure. The two groups do not differ significantly in either age or grade of tumor found.

Forty cases were considered inoperable; the patients either refused treatment, or were given palliative partial penectomy or radiation therapy. Thirty-four of the forty died of their disease within a year and four died of unknown causes within a year and a half. Two of the patients were apparently salvaged, one for 4 years and the other for 10½ years from the start of therapy. Both of these patients had partial penectomy plus x-ray therapy to the inguinal areas. The patient surviving 4 years died of an unknown cause at age eighty-eight. The patient surviving 10½ years had a grade 4 squamous cell carcinoma but was clinically free of tumor one month before he died of an unknown cause. The one patient in the entire series with a microscopic diagnosis of a sarcoma of unidentified type died 3 weeks after admission with marked local and inguinal extension of the tumor. Insufficient information was available for estimation of the relative palliative value in terms of comfort or longevity given by the various combinations of x-ray or radium therapy, with or without partial penectomy. All but three of the 40 cases, regardless of treatment, were dead within a year.

TABLE 3. *Grade of malignancy in 42 cases of squamous cell carcinoma of the penis*

Grade 1	13 (30.9%)
Grade 2	20 (47.6%)
Grade 3.	7 (16.6%)
Grade 4	2 (4.7%)

Of the entire series of 88 cases, forty-eight were treated with some chance of attaining cure. Twenty-six of this group died of their disease or surgery, eleven died of unknown causes or with the status of the tumor unknown, and ten were apparently free of tumor over 5 years after treatment. One additional patient died a cardiac death 1 year postoperatively and no tumor was found at postmortem examination. There were thirteen (27 per cent) of the forty-eight alive at the end of 5 years although two of them had evidence of metastases at that time and died a few months later. A third patient who had been treated by partial penectomy and extensive x-ray therapy to the inguinal areas was clinically free of tumor for 12 years and 4 months. At that time the right inguinal and femoral nodes rapidly enlarged and the patient died 4 months later, apparently of metastases.

For purposes of comparison, the types of treatment have been consolidated into three large groups. The first group of 15 cases had either partial penectomy at least 1½ cm. proximal to the lesion or complete penectomy with transplantation of the urethra to the perineum. A second group of 17 cases had the same surgical treatment plus x-ray or radium therapy to the inguinal areas. X-ray was administered to each inguinal area in amounts ranging from fifteen hundred to ten thousand tissue roentgens. A third group of 14 cases had partial or complete penectomy with bilateral resection of the inguinal lymph nodes. Nine of the fourteen patients in this last group had supplementary inguinal x-ray therapy. Apart from the three groups just mentioned, a single patient given x-ray and radium therapy alone died after 11 months with inguinal metastases. Another single patient with a pedunculated malignant melanoma had electrodesiccation of the lesion and died of heart disease 6 months later with the status of the tumor unknown.

The results of treatment have been tabulated separately for the three treatment groups previously outlined. Table 4, first column, shows that postoperative deaths, considered here to mean all deaths occurring within a period of one month after surgery, occurred four, two, and three times respectively for a total of 19.5 per cent of the 46 cases.

Table 4, second column, shows the number of patients in each treatment group who died of tumor or with tumor still clinically present. The figures are six, five, and five respectively for a total of 34.8 per cent. The average time of survival is shown in parenthesis. The 3½ year survival time of the 5 patients in the penectomy plus radiation group includes 1 patient who survived 12 years and 8 months.

TABLE 4

	POSTOPERATIVE DEATHS	DIED OF TUMOR	DIED—STATUS OF TUMOR UNKNOWN	DIED, OR LIVING FREE OF TUMOR OVER 5 YEARS
Penectomy, 15 cases	4 (26.6%)	6 (3 yrs. 1 mo.)	2 (11 mo.)	3 (20.0%)
Penectomy plus radiation, 17 cases	2 (11.7%)	5 (3 yrs. 6 mo.)	4 (2 yr. 4 mo.)	5 (29.4%)
Penectomy plus node resection, 14 cases	3 (21.4%)	5 (1 yr. 2 mo.)	4 (8 mo.)	2 (14.2%)
Total, 46 cases	9 (19.5%)	16 (34.8%)	10 (21.7%)	10 (21.7%)

Table 4, third column, records the number of deaths in each treatment group in which the status of the tumor was unknown, regardless of the clinically recorded cause of death. The totals for the groups respectively are two, four and four for a total of ten or 21.7 per cent. Again the average time of survival after first treatment is recorded in parenthesis.

Table 4, fourth column, shows the number of patients who were free of tumor over 5 years. Six died, free of tumor at periods of from 5 to 13 years after first treatment. Four patients are still living. Two in the penectomy group are alive at 6½ and 7½ years. One in the node resection group, whose inguinal nodes showed tumor bilaterally, is alive after 25 years. One in the penectomy plus radiation group is still living after 15 years and 3 months. The 5 year cure rate therefore in the three treatment groups combined is 21.7 per cent of the 46 patients. The numbers are too few for accurate estimation of the most effective treatment, but it is believed that better results are to be attained only by earlier diagnosis and extension of the indications for bilateral inguinal node resections. Radiation therapy probably should be reserved for palliation only.

Recurrence of tumor among the 48 patients who were treated with some chance of attaining cure occurred 21 times.

The time interval between first treatment and recurrence of tumor is shown in table 5. More than half of the recurrences were noted in the first postoperative year. Three recurrences were between the first and second years, two between the second and third years, and one each during the third and fourth years. One patient not listed had a recurrence recorded only as happening "several years" after therapy. The only recurrence found after 5 years was the one previously mentioned at 12 years and four months. Since recurrence of tumor after 5 years is a very rare happening, it is believed that the absence of tumor for 5 years after treatment is good evidence that cure probably has been attained.

TABLE 5. *Recurrence of tumor (21 cases among 48)**

	TIME OF RECURRENCE						
	Mo.		Yrs.				
	0–6	6–12	1–2	2–3	3–4	4–5	over 5
Number of cases....	7	5	3	2	1	1	1

* One case not listed.

SUMMARY AND CONCLUSIONS

A group of 88 cases of penile malignancy first diagnosed more than 5 years ago has been presented. Of the entire series 68.1 per cent eventually died of the tumor or its treatment, 19.3 per cent died of causes unrelated to tumor or with the status of the tumor unknown, and 12.5 per cent lived at least 5 years after treatment and were apparently cured.

Specific mention of the presence of phimosis was made in 53 cases. There were no recorded cases among those of Hebrew faith.

The age at which diagnosis was made ranged from 30 to 91. The average age was 60, and peak incidence in the age group 51 to 80.

Among 75 patients in the series, twenty delayed over a year in seeking medical advice. Physicians' error in diagnosis occurred with 10 patients and caused further delay of treatment an average of 11 months.

Inguinal adenopathy was found in 65 per cent of the total number of cases. Microscopic evidence of inguinal node metastases was found in 23 per cent of the total.

Among 40 patients who received no treatment or merely palliative treatment, all but two died within 1½ years. The remaining 2 patients died of unknown causes, apparently free of tumor, after 4 and 10½ years.

Among 48 patients who were treated with some hope of attaining cure by some combination of partial or total penectomy with or without radiation therapy and inguinal node resection, only 21.7 per cent lived over 5 years and were apparently cured.

It is believed that the poor results obtained can be improved by prompt biopsy of all darkfield negative penile lesions and by almost routine bilateral inguinal lymph node resections in addition to penectomy performed at least one and a half centimeters proximal to the lesion. Radiation therapy probably should be reserved for palliative treatment only.

The surgery and follow-up care have been done by several different urologists and radiologists and we are indebted to them, especially Dr. Bernard P. Widmann, chief of the Radiology Department of the Philadelphia General Hospital, for the privilege of the use of their records.

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FUNNEL AND BIB PLASTIC FOR HYPOSPADIAS. FOLLOW-UP EXPERIENCE

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Surgical correction of hypospadias has always been a difficult problem. Occasionally a new attempt is made with a newer and better plastic. But in spite of sincere efforts and intelligent management, the late results are just as disappointing as those obtained by the older methods. They all result in postoperative constrictions of the newly formed urethra and unless frequent dilatations are performed, complete occlusions ensue with formation of fistulas and return to the original preoperative state. A new approach and a better method are imperative.

In hypospadias we are dealing with a short urethra with the meatus in the middle or lower portion of the penis. Often chordee or downward curvature exists. The foreskin is always fully developed on the dorsal surface. No foreskin exists on the ventral surface. The entire ventral surface is covered with a thin layer of stretched out, glistening skin. There is no hair growth on the ventral surface of the penis. In order to void, the head of the penis has to be lifted up high by grasping the foreskin on the dorsum.

There are many ingenious ways to construct the new urethral tube. While all the techniques produce a sizable urethra on the operating table, its patency is lost later on. Sooner or later fibrous tissue forms, resulting in scar within the urethra and constricting bands outside the canal. Unless dilatations are practiced the tissue breaks down with the formation of fistulae. Once this occurs, the stream fails to reach the terminal meatus and spills out through the fistula. The new urethra above the fistula shrinks down because of disuse, and eventually closes off completely.

The ideal plastic operation for hypospadias would be a single surgical procedure that does not require postoperative urethral dilatations and permits normal urination; the cosmetic effect should be good. The funnel and bib plastic meets these requirements to the greatest degree. It has done so in our hands *continuously, uniformly, over a period of 15 years.*

We believe that the commonly practiced preoperative correction of the penile curvature is inadvisable. The removal of the so called "central tendon" is not only unnecessary but distinctly harmful. It destroys the smooth lining of the future roof of the new urethra. We believe this curvature to be due to the lack of complete enclosure of the penis by normal tissue rather than to a "central tendon." The truth of this conception can be demonstrated as soon as the urethral flap has been dissected. There is an immediate disappearance of the curvature and this without disturbing the base of the urethral roof and without dissecting any "central tendon." The late results surely prove the truth of this contention since the penis remains straight without any curvation whatsoever.

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The problem of locating the new meatus deserves careful consideration. In all the tubal plastics, the new urethra is brought up to the tip of the penis by tunneling the glans or by oversewing. This calls for obligatory postoperative dilatations. The insistence of placing the meatus at the head of the glans is the main reason for failure of many tubular techniques. Stricture formation within the glans is most common. Is it really necessary to do so? Why not avoid the glans completely? Why not bring the new meatus up to the glans and thus avoid the most serious constricting effect later on. Such a position of the new meatus is physiologically correct and voiding occurs with a straight and full stream. In trying to obtain a 100 per cent good cosmetic effect, one forfeits the entire procedure.

This operation is based upon the Ombrédanne principle. It consists of three steps: 1) suprapubic cystotomy; 2) preparation of the urethral ventral flap or funnel, and 3) preparation of the dorsal flap or bib.

TABLE 1. *Advantages of the flap over the tubular plastic*

	TUBULAR	FUNNEL
1. Number of operations	Multiple	One
2. Postoperative dilatations	Multiple, endless	None
3. Early results	Poor to fair	Excellent
4. Late results	Poor	Excellent
5. Cosmetic results	Fair	Good
6. Functional results	Poor to fair	Excellent
7. Length of convalescence	Long	Short
8. Admissions to hospital	Many	One
9. Financial expenditure	High	Low
10. Effect upon mentality	Poor	Good

SUPRAPUBIC CYSTOTOMY

A small buttonhole cystotomy is made. The only objector to a cystotomy is the one who looks upon this plastic as a minor correction of a minor deformity. Perineal drainage is not safe. It produces spasms and urination around the tube and down the newly formed urethra. The perineal tube may come out during sleep or while on the bed pan. Perineal drainage is therefore inadequate for the success of the plastic. The only safe and sure way to drain the bladder in these cases is by suprapubic cystotomy.

PREPARATION OF URETHRAL FLAP OR FUNNEL

The urethral flap is obtained by dissecting an area of skin from the ventral aspect of the penis. This glistening tissue is actually a thin epithelial covering closely resembling the fine mucous membrane of the urethra. It seems as if in the embryological stages there was an overproduction of the anlage of the urethral lining without an adequate urethral loge. The mucosa thus exuded from the hypospadic opening and overflowed the ventral surface of the penis like lava out of a volcano. The ingathering of this membrane by dissection with the help of a purse string stuture could thus be likened to a restorative process of normalcy.

In forming a new urethra the length of the flap should be two to three times as long as the distance from the coronal sulcus to the hypospadic meatus. It has to be so long because the dorsal skin is on stretch and becomes shorter and thicker as it is freed. Any apparent excess of tissue can readily be cut off at the end of the procedure. A small catheter is inserted in the meatus and moved down into the deep urethra without entering the bladder, thus avoiding the spilling of urine all over the wound. After measuring off the proper distance for the urethral flap, a marker is made by notching the skin at this point. An incision of about 1 cm. from the midline is then made parallel to the corpora cavernosae on the ventral surface of the penis on both sides beginning high at the corona down to the level of the lowermost marking. Once the edges of the flap are separated a few millimeters from the underlying tissue by sharp scissors dissection, the placement of the purse

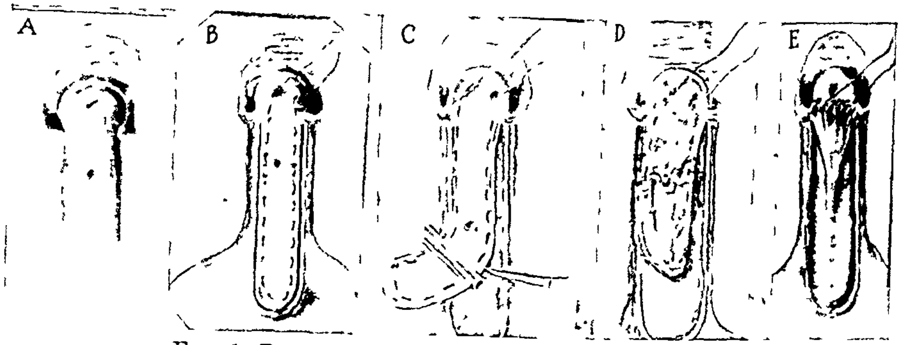

FIG. 1. Progressive stages of preparation of funnel

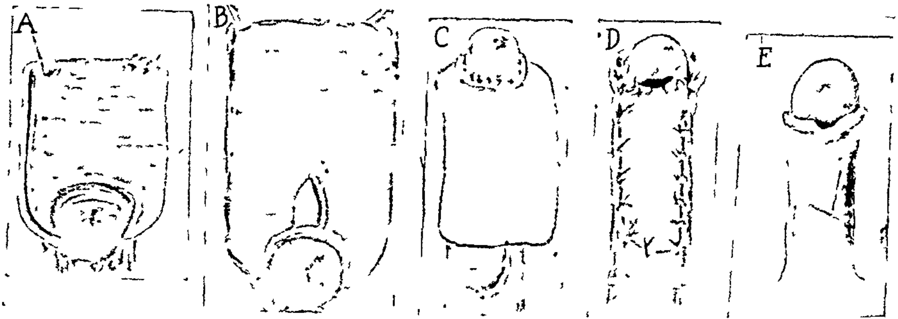

FIG. 2. Progressive stages of preparation of bib

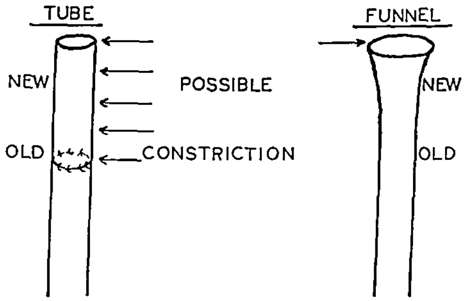

FIG. 3. Points of possible constriction in both tubal and funnel plastics

string suture is in order. Using 0000 chromic catgut on an atraumatic needle, the edges of the flap are picked up about every 5 mm. starting as high as possible on the ventral surface of the glans all along the right lateral margin downwards around the base of the flap and returning back upwards along the left lateral margin until the uppermost part of the glans is reached. The ends of the purse string sutures are held by a hemostat. The dissection of the flap proceeds further.

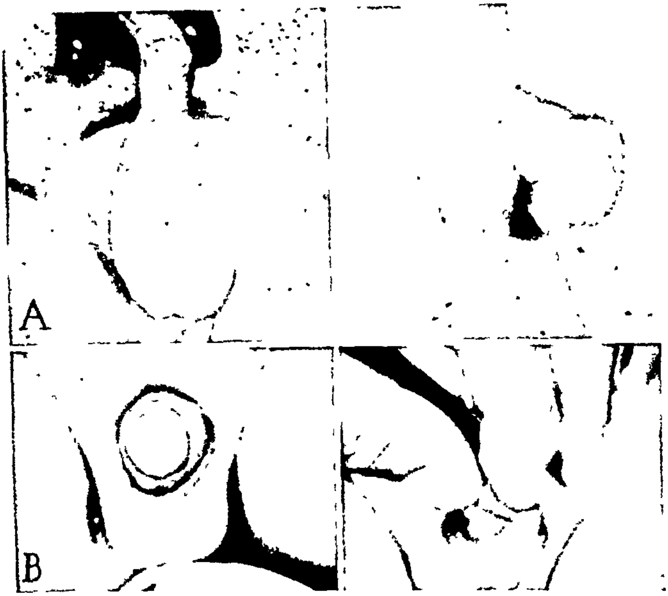

FIG. 4. Patient S. F. 3½ months postoperative. *A*, before operation. *B*, after operation.

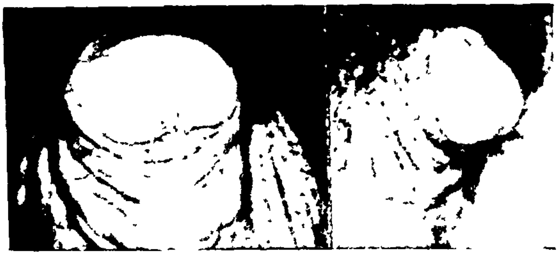

FIG. 5. Patient E. R. 7½ years postoperative

The purse string is drawn upwards by an assistant putting the flap on a stretch and thus greatly facilitating the sharp dissection. The bands of adhesions are cut until a smooth surface is obtained. Great care is taken to avoid the urethra proper. This is not difficult with the catheter in place. Before long dissection is complete. By pulling the purse string tightly upwards, one finds that the drawn up flap has formed a funnel-like structure in perfect continuity with the short urethra, the hypospadic meatus having completely disappeared inside of the funnel. The urethral opening is now at the corona. It appears as a puckered meatus held together by the purse string. At this point one realizes the soundness of this operation. It is not an addition or an anastomosis to the existing urethra requiring sutures which may or may not hold. The required length is added to the short urethra in complete continuity and with smooth epithelial lining on the inside. This funnel is about three times as wide as the short urethra. This caliber lessens later on and the funnel remains about twice as wide as the lower part of the urethra. There is no pathological reason or surgical chance for any constriction this point of natural junction. This, in our opinion, is the basic reason for the success of this procedure.

PREPARATION OF DORSAL FLAP OR BIB

This flap is prepared by lifting the foreskin which is always preserved on the dorsum of the penis. The majority of ritual circumcisers are aware of this and refrain from removing it. More educational work is needed to preserve the foreskin in these hypospadics. The foreskin is held in each corner with guy sutures put on stretch until flat. An incision is then made around the corona as in a regular circumcision. The incision is carried all the way around laterally until the raw surface of the ventral area is reached on both sides. The inner layer of the foreskin is then dissected upwards by using blunt scissors. Both layers of the foreskin are thus separated. The foreskin at this stage resembles a pocket. The lateral sides of the pocket are then cut. After this is accomplished one obtains a flat square piece of foreskin with a raw inner surface. Hemostats are applied to the upper corners of the square and the foreskin put on tension. A buttonhole incision is then made in the lowermost portion of the square piece of skin large enough to permit the slipping through of the head. The reason for making the buttonhole as low as possible is that by doing so the glans penis is held upwards preventing any future downward curvation. After the head is slipped through, the foreskin lies like a bib over the raw ventral surface of the penis. Interrupted sutures of 000 Dermalon are now placed around the dorsal part of the penis uniting coronal edge with the edge of the bib. Sutures are placed about every 5 mm. On the ventral side the rim of the buttonhole is united with the edge of the upward drawn urethral flap or funnel. There may be an excess of foreskin tissue on both sides of the head producing "ears". These excesses are cut off at this stage to conform with a proper cosmetic effect. The actual procedure is now completed. No catheter should be left in the urethra! We are careful to achieve an accurate approximation of the edges and are using interrupted sutures throughout. Dermalon seems to be the best material, being strong and dark in color. It is advisable not to tie the sutures too tight to prevent necrotic edges with superficial scab formation. If left alone such a scab drops off in 48 hours. We never saw any necrosis of the tissues.

The dressing is done with great care. A small piece of vaseline gauze—one layer 1 inch wide is placed around the penis, followed by a 1 inch gauze compression bandage. This bandage should not be too tight. A cross perineal figure of eight bandage (Blockley Binder) is then applied to include the cystotomy wound. Adhesive is used to reinforce the dressing and for fixation of the suprapubic tube.

The patient can be out of bed for short intervals several times a day. The dressing should not be disturbed for 6 days. At this date one finds the penis to be somewhat edematous. No sutures are disturbed. A new piece of vaseline gauze is applied; some local antiseptic may be used. The cross perineal bandage is reapplied. The suprapubic tube is left untouched. On the tenth day the very young patient is taken to the operating room for dressing and given some ethyl chloride or another general anesthetic for a short period. All sutures are removed gently with small instruments. The suprapubic tube is also removed and the patient may void through the new urethra. An apron dressing is applied to prevent chaffing. The older boys are sufficiently co-operative and permit suture removal without anesthesia. No urethral dilatations are needed postoperatively.

AGE OF SURGERY

This operation should be undertaken as early as possible. The patients usually become conscious of their inadequacy about the age of 5. Operating at a later age is not only inadvisable from a psychological standpoint, but becomes more difficult because of erections and uncontrollable emotional states.

FOLLOW-UP STUDIES

Our findings at the follow-up examinations were uniformally good. None had any postoperative treatment such as dilatation of the urethra or otherwise. All were voiding freely from the new meatus. None had any urethral fistulas. The meatus in all cases was wide open, about twice the size of normal. The meatus remained in the postoperative position. The organ itself was straight, firm and full. The ventral surface of the penis was well covered with a collar of tissue resembling a prepuce. All were voiding normally standing up. The oldest boys reported normal erection, straight and full without curvation. One of them has had normal coitus. In the older group the hair covered not only the shaft of the penis and scrotum but also the suprapubic scar. All boys appeared well developed physically and free from any mental inhibitions.

We have never encountered a case of hypospadias without the dorsal foreskin. However, should this be the case it would not interfere with the proper preparation of the funnel or urethral flap. The only problem would be the missing bib or the covering of the exposed ventral raw surface. It should not be difficult to swing a skin flap from the scrotum to cover this defect since there is ample loose scrotal skin to choose from.

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PRECOCIOUS PUBERTY IN A CASE OF BILATERAL INTERSTITIAL CELL TUMOR OF THE TESTES

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It is the purpose of this paper to report an unusual and extremely interesting case of bilateral interstitial cell tumor of the testes exhibiting precocious puberty at the age of 3 years. This paper is concerned only with those tumors found in children.

Interstitial cell tumor of the testicle is a rare disease. This case was the only one seen at the Roswell Park Memorial Institute in a period of 37 years, during which time 75,285 patients were admitted. During this same period 258 testicular tumors were treated.

CASE REPORT

J. W. (No. 24613—B.C.H.—No. 69929—R.P.M.I.) was first seen at the Buffalo Children's Hospital on June 13, 1931 at the age of 1 year and a diagnosis of rhinopharyngitis was made. No abnormalities of the external genitalia were found.

On August 1, 1933 the patient was again seen at the Buffalo Children's Hospital when he was 3 years old. The father complained that for a period of 6 months the youngster had several erections throughout the day and appeared to be masturbating frequently. Physical examination revealed that the child was large for his age. His hands and feet appeared larger than normal. Pubic hair was present and the penis was enlarged (fig. 1, *A*). The remainder of the physical examination was negative. X-ray of the skull was normal with an average size sella of open type without erosion. The epiphyses of the long bones showed abnormal development equivalent to a seven year old.

He was seen again 1 year later on October 2, 1934 at the age of 4 years and at that time appeared to be 8 years old. He was very restless and the parents found him difficult to manage. The child was admitted for a tonsillectomy, and physical examination showed the presence of pubic hair and an adult sized penis (fig. 1, *B*). (No measurements were taken.) Excretory urograms demonstrated no evidence of disease. A repeat x-ray of the sella showed a normal sized sella with regular outline. Funduscopic examination was normal. A glucose tolerance test revealed levels as follows: Fasting 75 mg.; ½ hr. 129 mg.; 1 hr. 108 mg.; and 2 hrs. 84 mg.

Psychometric examination was done on May 31, 1935 when the child was 4 years and 11 months old, and this revealed an I.Q. of 92. On September 16, 1935, at the age of 5 years and 2 months, he weighed 68 pounds and was 54⅛ inches tall, having grown 4 inches in the previous 9 months. On March 12, 1936 he weighed 79 pounds and was 55.8 inches tall, and at that time an exploratory laparotomy was advised to investigate the possibility of an adrenal tumor. This

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request was refused by the parents. On May 29, 1936 when he was 5 years and 11 months of age (fig. 1, *C*) his mental age was 6 years and 4 months, giving him an I.Q. of 107 by the Stanford-Binet test. A Goodenough drawing gave the test age of 7 years and 6 months. On February 11, 1937, at the age of 6 years and 7 months, x-rays taken of his wrist and knees revealed the bony development of a boy 15 years old.

On October 11, 1941 he weighed 127½ pounds and was 63.4 inches tall. He appeared to be 17 years old, whereas he was actually 11 years and 3 months of age (fig. 1, *D*). He had hair on his chest and extremities. His voice had changed and acne appeared on his face. The genitalia were fully developed. The testes had a completely abnormal feel, being firm, stony hard and nodular, bilaterally. This admission was the first time that mention was made concerning the abnormality of the testicles. He was last seen at the Buffalo Children's Hospital in 1943 when a mastoidectomy was performed. Following this he had no further admissions or studies of his hypergonadism.

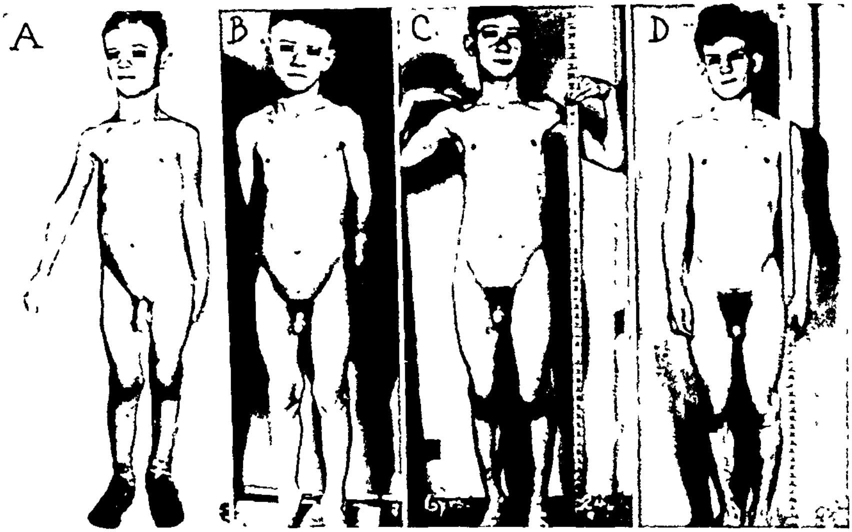

FIG. 1. *A*, photograph of patient at age 3 years. Note beginning enlargement of external genitalia. *B*, at age 4 years. Note macrogenitosomia and pubic hair. *C*, at age 6 years. Note accelerated bone and muscular development. *D*, at age 10 years. Note hirsutism of lower extremities and adult genitalia.

During the course of a pre-employment examination the physician noted bilateral enlargement, nodularity and hardness of the testicles, and referred him to to the Roswell Park Memorial Institute where he was seen September 15, 1950. He had no complaints referable to any of his systems.

Physical examination revealed a well nourished, well developed white 20 year old man not acutely ill. The examination was negative except for bilateral enlargement, nodularity and stony hardness of the testes. Neither testis transilluminated and they were quite heavy. Temperature was 98.6F, pulse 70, respiration 18 and blood pressure 120/80. Urine: alkaline; specific gravity 1.020; albumin: negative; sugar, negative; microscopically: rare squamous cell; white blood cell 2–3 per high power field. A sperm sample was obtained following ejaculation and the total volume was 2.5 cc. The color and viscosity were normal. Examination revealed no sperm present in either the hanging drop, stained smear or on the counting chamber following dilution with Locke's solution. Hemoglobin, 14.95 gm.; red blood cells, 5,600,000; white blood cells, 8,800; differential count: eosinophils 5 per cent; stab polymorphonuclears 8 per cent; segmented polymorphonuclears 47 per cent; Lymphocytes 40 per cent. Blood chemistry: Sugar 85 mg. per cent; nonprotein nitrogen, 35 mg. per cent; serum albumin, 5.31 per cent; serum globulin, 1.53 per cent; whole blood chlorides, 442 mg. per cent; acid phosphatase, 3.2 King Armstrong units; alkaline phosphatase, 8.3 King Armstrong units urine, 17 ketosteroids preoperative: 1) October 4, 1950, total 39 mg./24 hours; 2) October 5, 1950, total 52 mg./24 hours; 3) October 27, 1950, total 73.9 mg./24 hours. Alpha 72.0 mg./24 hours; beta 1.2 mg./24 hours (table 1). Aschheim-Zondek test: October 5, 1950, volume 1920 cc, negative in all concentrations. Urine culture: bladder urine, sterile; left kidney: sterile; right kidney: sterile; 24 hour concentrated urine for tuberculosis was reported as negative on smear, culture and guinea pig innoculation.

TABLE 1. *Urinary 17-ketosteroid determinations per 24 hours*

	DATE	TOTAL	ALPHA	BETA
I. Preoperative				
	10–4–50	*39 mg.*	*Not determined*	*Not determined*
	10–5–50	52 mg.	Not determined	Not determined
	10–27–50	73.9 mg.	72.0 mg.	1.2 mg.
II. Postoperative				
A) 1st p.o. day	11–9–50	113.5 mg.	108.8 mg.	5.3 mg.
B) 2nd p.o. day	11–10–50	162.0 mg.	153.8 mg.	5.9 mg.
C) 3rd p.o. day	11–11–50	141.0 mg.	135.5 mg.	6.7 mg.
III. Follow up				
	1–8–51	104.6 mg.	100.0 mg.	4.6 mg.
	2–6–51	157.3 mg.	150.2 mg.	7.45 mg.
	2–20–51	69.6 mg.	67.6 mg.	2.6 mg.

X-ray of the chest was reported as negative. Bilateral retrograde pyelograms were taken. The flat film of the region of the kidneys, ureters and bladder with ureteral catheters inserted bilaterally showed the soft tissue shadow of the kidneys to be of normal size and in normal position. No calculi were seen in that region. Films taken after the retrograde injection of diodrast showed the kidney pelves and calyces to be well outlined and normal on both sides. A perirenal air insufflation outlined both kidneys well with no indication of adrenal gland enlargement. An anteroposterior and lateral x-ray of the scrotum showed no evidence of calcification of either testicle.

Operation: Left orchiectomy (W. J. S. and M. S. B.) on October 28, 1950. The postoperative course was uneventful. Pathological report, No. 302222 (E. M.

Burke): The gross specimen consisted of the left testicle and cord. The testicle measured 7 by 4 by 3½ cm. The testicular substance showed replacement by firm, brown, nodular masses (fig. 2, *A*).

Microscopic sections showed a tumor composed of interstitial cells found in cords. The nuclei showed considerable variation in size. In some areas the tumor cells were compressed by fibrous tissue but for the most part grew in solid cords. Some atrophic testicular tubules were found. There was no change suggestive of malignancy (fig. 3, *A* and *B*).

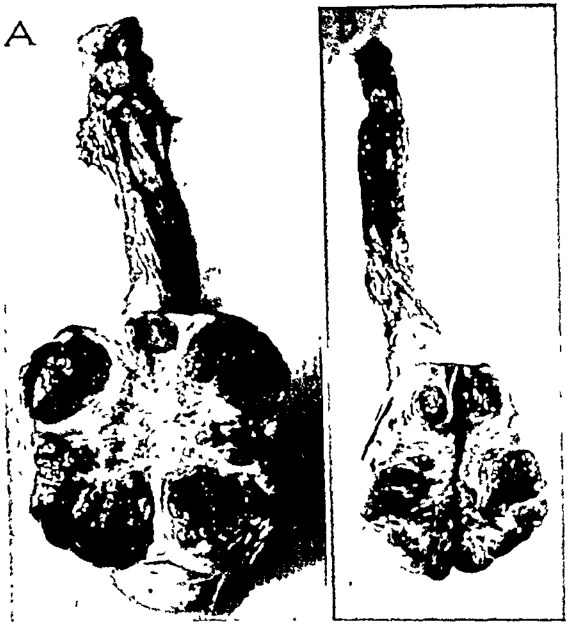

Fig. 2. Cross section of gross specimen of left testicle with its attached cord showing discrete tumor nodules. *B*, cross section of gross specimen of right testicle and its attached cord showing nodular masses of tumor and fibrosis.

Operation: Right orchiectomy (W. J. S. and M. S. B.) on November 8, 1950. The postoperative course was uneventful. Pathological report No. 302406 (E. M. Burke): The gross specimen consisted of the right testicle and cord. The testicle measured 6½ by 3 by 4 cm. The testicular substance was replaced by firm, brown, nodular masses (fig. 2, *B*).

Microscopic sections showed a tumor composed of large cells of the interstitial type with considerable variation in the size of the nuclei, while in many areas the tumor grew in solid masses and cords. In other areas there was a marked fibrosis separating the tumor cells into small nodules. There was no change suggestive of malignancy (fig. 3, *C* and *D*).

Postoperative 17-ketosteroid determinations (table 1): first postoperative day (November 9, 1950), total 113.5 mg./24 hours; alpha 108.8 mg./24 hours; beta 5.3 mg./24 hours; second postoperative day (November 10, 1950), total 162.0 mg./24 hours; alpha 153.8 mg./24 hours; beta 5.9 mg./24 hours; third postoperative day (November 11, 1950), total 141.0 mg./24 hours; alpha 135.5

mg./24 hours; beta 6.7 mg./24 hours. The patient was discharged November 20, 1950.

Follow up, January 8, 1951: The patient had no complaints. Both incisions had healed well. His libido had not been altered. A 17-ketosteroid determination on a 24 hour collection of urine was obtained. This was reported as: total—104.6 mg./24 hours; alpha 100.0 mg./24 hours; beta 4.6 mg./24 hours. On February 6, 1951 another urinary 17-ketosteroid determination was reported as: total—157.3 mg./24 hours; alpha 150.2 mg./24 hours; beta 7.24 mg./24 hours. The patient was last seen on February 20, 1951 and he enjoyed good health. Urinary 17-ketosteroids on a 24 hour urine collection obtained at that time was reported

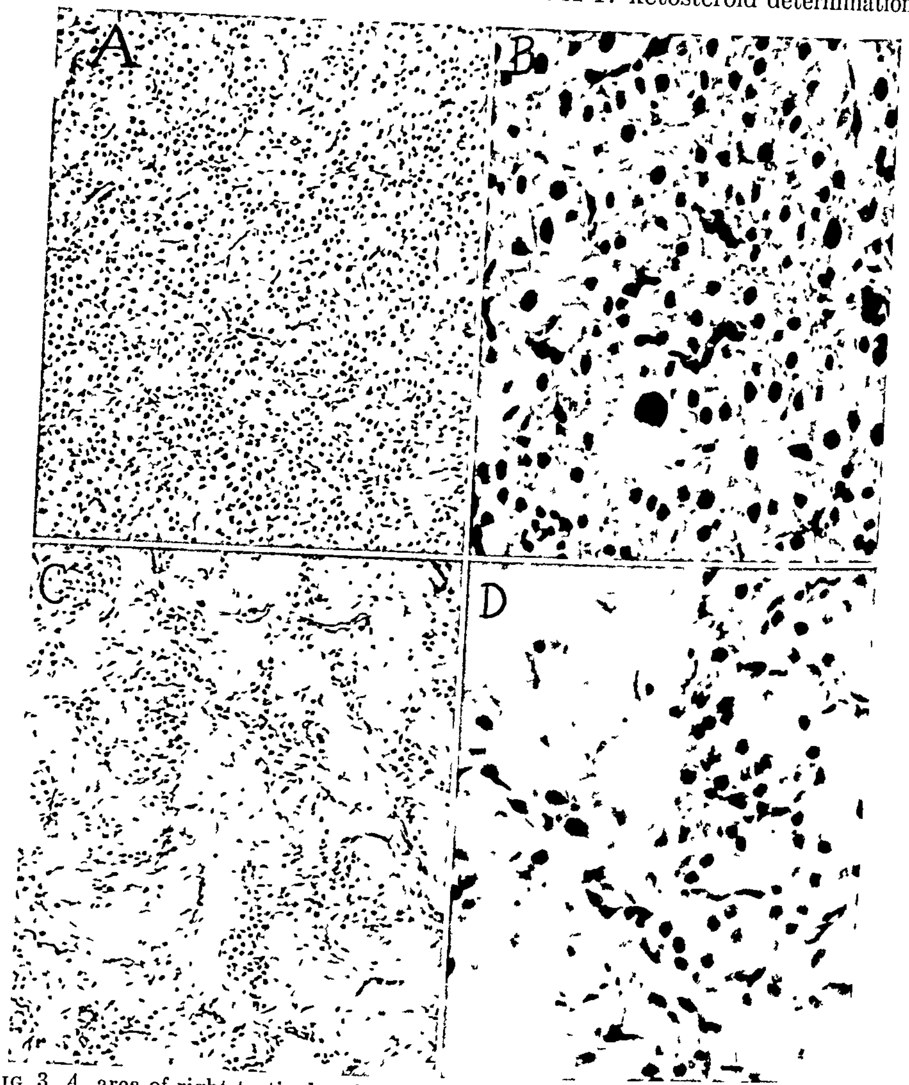

FIG 3. *A*, area of right testicular tissue showing diffuse overgrowth of interstitial cells. ×100. *B*, from right testicle showing variation in size of nuclei of interstitial cells. ×250. *C*, from left testis showing strands of tumor cells separated by increased fibrosis. ×100. D, from left testis showing in detail extreme fibrosis with nest of tumor cells

as: Total—69.6 mg./24 hours; alpha 67.6 mg./24 hours; beta 2.6 mg./24 hours (table 1).

This patient was inducted into the United States Army in March 1951, and at present is a member of the Armed Forces.

REVIEW OF THE LITERATURE

Leydig in 1850 first described the interstitial cells of the testes. The first reported tumor of this type was published by Sacchi[1] in 1895. Since this initial report, 10 cases of interstitial cell tumors in children have appeared in the literature. These have all been unilateral.

Sacchi[1] of Genoa, Italy in 1895 reported a case of a 9 year old boy who had the appearance of a young man. There was excessive skeletal and muscular development. The skin showed an abundance of hair and the beard was 5 cm. in length. The patient was a normal boy until age 5— years when he began to exhibit precocious puberty. The left testicle became larger than the right and was removed. One month after operation the beard and the hair on the arms and legs fell out and the voice became childish. Four months postoperative the beard disappeared. There was no regression in the muscular or skeletal development. The histology of the left testicle was that of an interstitial cell tumor.

Rowlands and Nicholson[2] in 1929 at Guy's Hospital, London reported a case of a boy 9 years of age with enlargement of the left testicle and premature puberty. The patient was normal until 6 years of age when his growth became rapid. The voice deepened and at 8 years he had the appearance of an 18 year old. He was 5 feet tall and well built. There was hair on the chest, loins and pubis. The left testicle was removed and found to contain an interstitial cell tumor. He was seen 2 years postoperative and there was no regression in the signs of puberty. The patient was 11 years old then, shaved regularly, and had grown three-fourths of an inch in height in 2 years.

Stewart, Bell and Roehlke[3] in 1936 reported a case of a 5 year old boy who was normal until age 5 when he began to exhibit the phenomena of puberty. He developed pubic hair and his voice deepened. A small tumor was palpated in the right testicle. A right orchiectomy was performed and an interstitial cell tumor was found. Following surgery there was disappearance of the axillary and pubic hair and the voice became childish.

Somerford[4] in 1941 from the Manchester Children's Hospital, England reported a case of an 11 year old boy who had precocious puberty, marked muscular development and a history of an enlarged right testis for 6 years. The right testicle was removed and an interstitial cell tumor was found. After operation the boy was kept under observation for 18 months but the secondary sexual characteristics showed no signs of regression.

Huffman[5] in 1941 reported a case of a 6 year old boy who complained of swelling of the left testicle. Two years previously a playmate kicked him in the scrotum and since then there had been gradually increasing swelling and slight tenderness of the left testicle. A moderate growth of pubic hair had occurred and there was slight enlargement of both breasts. The child was advanced in physical development. He was 51 inches tall and weighed 60 pounds. An orchiectomy was performed and an interstitial cell tumor of the left testicle was found. He was seen 2 years postoperative and appeared to be a normally developing boy except that the enlargement of the breasts and growth of pubic hair had persisted as before operation.

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[1] Sacchi, E.: Rivista Sperimentale di Freniatria e di Medicina Legale, Reggio, 21: 149, 1895.

[2] Rowlands, R. P. and Nicholson, G. W.: Guy's Hospital Reports, 79: 401, 1929.

[3] Stewart, C. A., Bell, E. T. and Roehlke, A. B.: Am. J. Cancer, 26: 144, 1936.

[4] Somerford, A. E.: Brit. J. Urol., 13: 13, 1941.

[5] Huffman, L. F.: J. Urol., 45: 692, 1941.

Werner et al.[6] from St. Louis in 1942 reported a case of a 6 year old boy with macrogenitosomia, pubic hair and an adult male voice. He was 6 inches taller and 20 pounds heavier than normal for his age. The muscles were overdeveloped and firm. Roentgenograms showed advanced bone development. The right testis was enlarged. This was removed and was diagnosed as an interstitial cell tumor. Three and one half months postoperative there was regression of the abnormally developed secondary sex characteristics.

Melicow et al.[7] in 1949 reported a case of a 5 year old boy with precocious sexual development. The voice was adult male in character. Pubic hair was present and the child appeared older than his stated age. The penis and scrotum were of adult size. A large right testis which did not transilluminate was present. This was removed and a diagnosis of interstitial cell tumor was made. No regression was noted after 6 months.

The following 3 cases also appeared in Melicow's review of the subject in 1949. We were unable to find any other reference to them in the literature.

1) The case of Masson's in 1941 was that of a 9 year, 7 months boy who appeared to be 18 or 19 years of age. The penis was enlarged and hair was present on the chest, axilla and pubis. The voice was adult male in character. A left orchiectomy was performed and an interstitial tumor was found. Follow-up examination revealed metastases to the liver. This case represents the only reported malignant tumor found in children.

2) Rezek in 1943 had a 10 year old boy who appeared to be 18 and was heavy muscled. The penis was enlarged and the voice was adult male in character. Hair was present on the chest, axilla and pubis. The left testicle was removed and an interstitial cell tumor was found. No report on the follow up was available.

3) W. D. Anderson in 1946 reported a case of a 6 year old boy who smoked cigars and was heavily muscled. He had axillary and pubic hair. A right orchiectomy was performed and a yellow-gray oval tumor was found. The main symptoms regressed after operation.

DISCUSSION

The gross appearance of interstitial cell tumors is usually characteristic. The size of the tumor is variable. In most cases, the growth is surrounded by a fibrous capsule and is nodular and yellow-brown in color. In carcinoma where cellular differentiation is less advanced the color may be blue-gray, as in Masson's[8] case. The yellow-brown color is due to the lipids contained within the cells.

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[6] Werner, A. A., et al.: J. Clin. Endocrinal., **2:** 527, 1942.

[7] Melicow, M. M., et al.: J. Urol., **62:** 672, 1949.

[8] Masson, P. and Sencert, L.: Bull. d. l'Assoc. Franc. p. l'étude du cancer, **12:** 556, 1923.

Microscopically the tumor consists of large polyhedral cells. These are found in sheets or lobules separated by a collagenous stroma.

The cytoplasm in the more differentiated cells is loaded with brown granules, thought to be waste pigment, and crystalloids of Reinke, which are rod shaped bodies with rounded or pointed ends. The latter are not always present. The cytoplasm also contains mitochondria and refractile bodies.

The nucleus is large and usually spherical and contains one or two large nucleoli and numerous coarse granules. Binucleate cells are not uncommon and multinucleated cells may be found.

Up to the present time there has been no definite criteria for the differentiation of normal states of the interstitial cells from hyperplasia. Too little has been known of normal variations in the interstitial cellular component of the testicle for a clear cut division. It is believed that hyperplasia may be due to the diminished spermatogeneses which takes place in chronic diseases, injury, castration, cryptorchidism, exposure to x-ray or radium emanations, environmental changes or drug administration. The number of interstitial cells from fetal life to senility tend to correspond inversely with changes in spermatogenesis. However, in evaluation of hyperplasia, one must realize that large collections of interstitial cells are not necessarily pathologic nor does the presence of multinucleated cells or cells in the tunica albugines and epididymis indicate invasion.

Except for the presence of metastases no definite criteria for the determination of malignancy has been found. Mitoses and cell irregularity have been noted in hyperplasia and benign tumors as well as in carcinoma. As a matter of fact, two of the reported cases of carcinoma[8, 9] failed to reveal any mitotic figures.

The hormonal changes resulting from interstitial cell tumor of the testes are very interesting. Between the seminiferous tubules of the testicles in the loose connective tissues are the interstitial cells or cells of Leydig. These may occur alone or in clumps. It is generally believed that testosterone, which is necessary for the development of the male secondary sex characteristics and sexual instincts, is derived from these cells as an internal secretion. In the normal individual these cells do not function actively until puberty, at which time they are stimulated by the luteinizing hormone of the anterior lobe of the pituitary and cause development of secondary sex characteristics.

In the male the urinary excretion of 17-ketosteroids appears to be dependent upon the activity of the adrenal cortex and the testes. These urinary 17-ketosteroids can be separated into two groups, the alpha and the beta, depending upon the spacial configuration at the C-3 and C-11 positions. The adrenal cortex is presumed to be the sole source of dehydroisoandrosterone, one of the members of the beta fraction. A change in the quantitative excretion of dehydroisoandrosterone and the resulting change in the beta fraction is therefore generally indicative of adrenal cortical mal function.

On the other hand, the interstitial cells, or cells of Leydig, are presumed to produce androgens which contribute to the excretion of the alpha 17-ketosteroids. Hypofunction of these cells does not necessarily lower the amount of 17-ketosteroids excreted below normal levels since the spread of normal excretion is

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[9] Masson, P.: Rev. Canad. de biol., 1: 571, 1942.

rather broad and the adrenal cortex produces the predominant amount of this material. There also exists the possibility that the adrenal cortex becomes stimulated and produces more of the 17-ketosteroids when hypofunction of the interstitial cells occurs.

Hypersecretion of testicular androgens results in an increased output of 17-kestoteroids. In Venning's[10] case the 17-ketosteroids rose to 1015 mg./24 hour sample of urine. There were extensive metastases present and these could account for the greatly increased excretion.

The urinary 17-ketosteroid findings in the case reported are difficult to rationalize. We have been unable to determine the cause of the markedly increased excretion of alpha and beta urinary 17-ketosteroids postoperatively. Initially the possibility of increased metastatic activity was considered. However, the decline in both fractions over a 4 month period seem to preclude this possibility and indicate that further research into the metabolism of adrenal and testicular hormones must be undertaken before the answer to this problem can be found.

The symptomatology exhibited by the 10 cases of interstitial cell tumor found in children is very interesting. All showed macrogenitosomia, pubic hair, adult male voice and accelerated bone and muscular development. The age of onset of symptoms ranged from 4 years to 5½ years. In the case we are reporting the onset of symptoms occur at the age of 3 in the form of frequent erections, macrogenitosomia, pubic hair and accelerated bone and muscular development. No mention was made of voice changes until age 11.

Following the removal of the involved testicle, there was regression of hirsutism in 4 cases and reversion of voice change in two. The remaining cases showed little or no regression. Orchiectomy was not performed in our case until age 20 and the only change noted occurred in the urinary 17-ketosteroid determination. There was a rapid rise immediately postoperative and follow-up determinations have shown a gradual decline.

Treatment consists of orchiectomy and careful follow-up examinations which should include urinary 17-ketosteroid excretory studies. Since metastases occurred after 9 years in Masson's case, it seems that patients with interstitial cell tumors should be observed for at least 10 years. This is especially important if in the original growth some of the seminiferous tubules were destroyed.

SUMMARY

The first case in the literature of bilateral interstitial cell tumor of the testes manifesting precocious puberty at age 3 is reported.

A follow up from age 3 to 20 is presented.

A review of the literature of 10 cases is reported.

A discussion of the pathology, physiology, symptomatology and treatment was made.

The authors express their thanks to Dr. A. Wilmont Jacobsen, Clinical Professor of Pediatrics, University of Buffalo, School of Medicine for valuable suggestions concerning this case. The patient was under Dr. Jacobsen's supervision while at the Buffalo Children's Hospital.

[10] Venning, E. H.: Rev. Canad. de biol., 1: 571, 1942.

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THE INTRARENAL PRESSURE DURING DIURESIS AND ANTIDIURESIS

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Winton (1933) has reported that the intrarenal pressure rises during diuresis. His method of measuring intrarenal pressure entails the determination of the ureteral pressure which just slows the flow of urine out of the kidney. This method, however, appears somewhat indirect: with more direct techniques, we (Montgomery, Davis, Prine and Swann, 1950; Swann, Hink, Koester, Moore and Prine, 1952) have found the intrarenal pressure to be normally at 25 mm. Hg, rather than at 10 mm. as reported by Winton (1937). Using the new techniques, the problem of the intrarenal pressure during diuresis has accordingly been re-investigated.

METHODS

To measure intrarenal pressure (to be abbreviated IRP), the transduced equilibrium method of Swann, Montgomery, Davis and Mickle (1950) was used. A diagram of the apparatus is shown in figure 1. A cannula (actually a 20-gauge needle) with lateral holes is thrust into the renal parenchyma. This is connected with a nearly isometric manometer which is stretched with a small volume of saline (about 5 cmm.). The manometer is then allowed to discharge its contents through the cannula and into the kidney tissue. As the manometer forces fluid into the kidney, its pressure rapidly falls; when it stops discharging fluid, the pressure in it is presumed equal to the IRP. Because it has recently been shown that the intrarenal venous pressure is also 25 mm. Hg (Swann, Hink, Koester, Moore and Prine, 1952), the validity of our present method of measuring intrarenal pressure has received strong confirmation.

Two improvements have been made in the apparatus since it was first described. The stop-cock by which the pressures in the system are controlled tends to leak. But since fluid must escape from the system only out of the cannula, such a leak invalidates any measurements taken. It was found that a mercury-sealed cock effectually rectified the tendency to leak. Therefore, the stop-cock itself and all its three entrances were filled with mercury. A reservoir to collect the small volume of mercury that accumulates with each discharge of the apparatus was also found desirable.

Both anesthetized and unanesthetized dogs were employed. The anesthetic was sodium pentobarbital. One kidney was exposed and a ureter cannulated; then the IRP and urinary flow rate were ascertained during an induced diuresis. The carotid arterial blood pressure was also usually measured during the experiment. To study diuresis without anesthesia, female dogs were prepared: the right kidney was removed surgically and the left kidney explanted to a subcutaneous position in the flank. After a month or more of recovery, the dogs having mean-

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while been trained to lie quietly, the urinary flow rate and IRP were determined simultaneously during diuresis. The needle cannula used to measure IRP was thrust through the skin and into the renal parenchyma. To measure urine flow, the dog's bladder was catheterized. In some of these dogs, the IRP during pituitrin antidiuresis was also ascertained.

In many of the experiments on anesthetized dogs, the pressure in the renal arcuate veins was also ascertained. This measurement, as discussed above, has recently been found to furnish good confirmation of the measurements made by the transduced equilibrium method, for the two, when taken simultaneously, agree well in a variety of experimental conditions. For the sake of completeness, therefore, it was occasionally used in these experiments on diuresis.

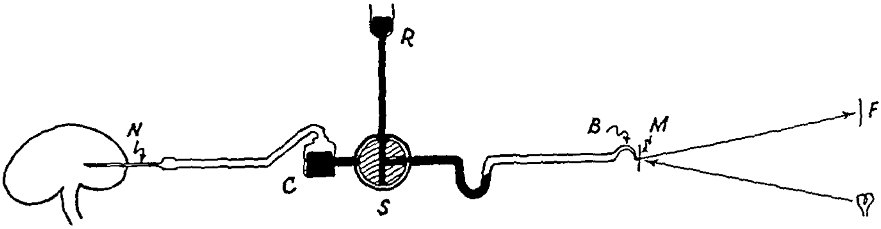

FIG. 1. Apparatus for measuring tissue pressure. Manometer B is stretched by opening stop-cock S to mercury column R. Then stop-cock is turned 90° clockwise and stretched manometer allowed to discharge. It pushes small volume of mercury into collecting reservoir C which in turn forces small volume of saline into kidney through needle N. Pressure in manometer is registered optically by mirror M and film F.

RESULTS

A. Anesthetized dogs. Figure 2 shows a typical experiment, including measurements of blood pressure, urinary flow, intrarenal pressure and renal arcuate venous pressure during a urea-induced diuresis. The urea was given intravenously; it caused a 12-fold increase in urine flow; the peak urine flow was 1.9 ml./min. at 15 minutes. After a brief hypotension, due to the toxic effect of suddenly injecting concentrated urea solution, the blood pressure leveled off at about the preinjection level. The intrarenal pressure and the arcuate venous pressure agreed well: both rose sharply to about 60 mm. Hg as the diuresis developed. Then they fell slowly to the preinjection level after 15 minutes. The latter fall occurred in spite of the continuing diuresis.

Table 1 shows the data for 20 anesthetized dogs, given intravenous, diuretic injections of glucose, urea, sodium sulfate or saline. Although there was considerable individual variation in reaction, nonetheless all followed the general pattern described in the protocol of figure 2: little or no change in blood pressure, after a brief period of toxic hypotension, about a 10-fold rise in urine flow, a sharp rise in IRP to 50–60 mm. Hg, then a fall in the latter, often before the subsistence of the diuresis. In table 1, these data are summarized, with maximum urine flows and IRPs indicated. The highest urine flow usually occurred some minutes after the peak IRP had been observed. In the last column of the table, the range of peak IRPs is shown. In a few dogs, the IRP did not rise greatly; in most it rose abruptly to about twice the control value. In 4 out of the 20 dogs, the peak

IRP exceeded 70 mm. Hg; in one it rose to 92 mm. Hg. As previously mentioned, arcuate venous pressures were also measured in occasional experiments. They agreed well with the simultaneously measured IRPs.

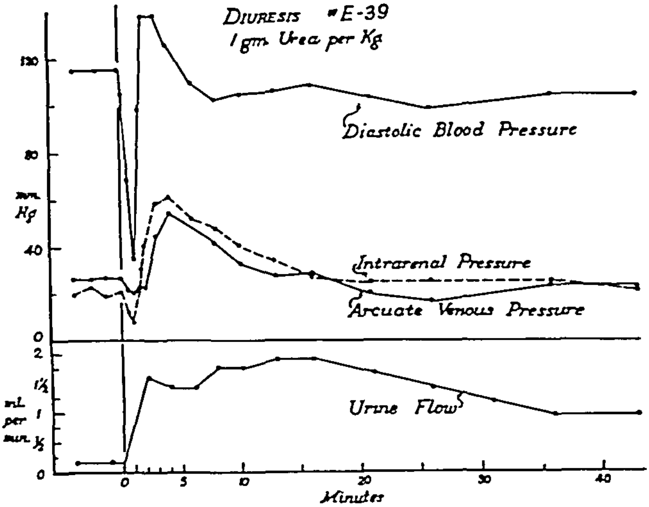

FIG. 2. Effect of urea diuresis on intrarenal and arcuate venous pressure

TABLE 1. *Effect of diuresis on intrarenal pressure*

DIURETIC (INTRAVENOUS)	NO. OF DOGS	AVERAGE URINE FLOW, ML./MIN. Preinjection	AVERAGE URINE FLOW, ML./MIN. At peak diuresis	AVERAGE IRP, MM. Hg Preinjection	AVERAGE IRP, MM. Hg At peak IRP	RANGE OF PEAK IRPs, MM. Hg
Na Pentobarbital						
Glucose, 1 gm./Kg.	7	.1	1.1	25	50	38–73
Urea, 1 gm./Kg.	6	.2	1.1	25	58	21–87
Na_2SO_4, 2 gm./Kg.	3	.1	2.2	20	48	34–72
.9% NaCl, 20 ml./Kg.	4	.1	.7	31	62	46–92
Unanesthetized						
Glucose	7	.4	3.1	22	22	9–40
Urea } same doses	3	.6	2.6	15	16	12–25
.9% NaCl	2	1.4	1.6	28	32	20–43
Water, *per os*, 40 ml./Kg.	14	.4	4.1	20	31	20–46

B. Unanesthetized dogs. Diuresis in the anesthetized dogs causes, as shown above, a sharp rise in IRP. But by contrast, in the absence of anesthesia, diuresis does not cause any noteworthy change in IRP. Table 1 assembles the data for 26 experiments, performed at different times upon a group of 5 dogs with kidney explants. Glucose, urea or saline, given intravenously at the same dose levels as used on anesthetized dogs, invoked a considerable diuresis in these animals; greater absolute flows, in fact, than with the anesthetized animals. But the while been trained to lie quietly, the urinary flow rate and IRP were determined simultaneously during diuresis. The needle cannula used to measure IRP was thrust through the skin and into the renal parenchyma. To measure urine flow, the dog's bladder was catheterized. In some of these dogs, the IRP during pituitrin antidiuresis was also ascertained.

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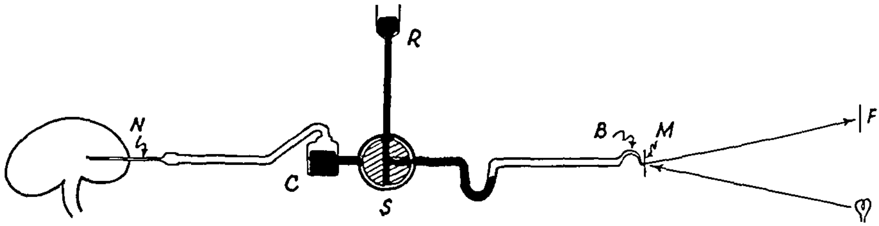

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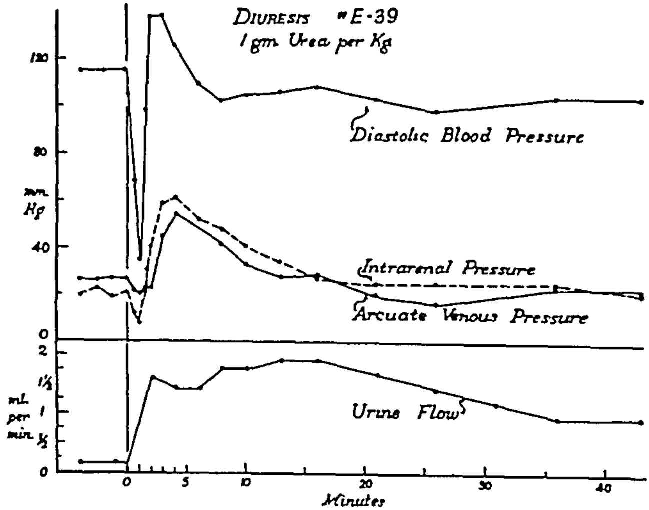

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IRP did not rise sharply as before. A few dogs experienced slight rises, a few slight falls in IRP. On the average, as the table shows, the diuresis was not accompanied with any change in IRP.

Water, given by stomach tube, was also tested (table 1). It invoked a great diuresis; it also caused on the average a rise in IRP of 11 mm. Hg. This increase, however, is small; it was also inconstant, taking place in only 10 of the 14 experiments. We may therefore conclude that the tendency for the IRP to rise is small and insignificant.

C. Antidiuresis. In seven experiments, at the height of a water-induced diuresis, the dogs were injected subcutaneously with 0.5 ml. of pituitrin (pituitrin (S), 10 international units). This caused an abrupt drop in urine flow from the observed preinjection level of 5.2 ml./min. to a level of 0.6 ml./min. some 10 minutes later. During this time, the IRP fell on the average from its mildly elevated level of 36 mm. Hg to 30 mm. Again, the data were unconvincing. During strong antidiureses, it is clear that although a fall in IRP occurs, it is small and insignificant.

DISCUSSION

The very high interstitial pressure at which the kidney can operate is noteworthy. Even though its interstitial pressure is 70 mm. Hg, it functions satisfactorily as shown by the observation that urine is still formed. The tenseness of the kidney when diuretic is equalled, to our best knowledge, by only one other organ in the body, viz. the eye in glaucoma, when intra-ocular pressures of 60–90 mm. Hg are reached. Even maximally tensed muscles do not often have interstitial pressures much greater than 50 mm. Hg (Wells, Youmans and Miller, 1938). Another facet of this fact of operation at very high tissue pressures is to be found in the data on "maximum ureteral pressures": the ureteral pressure required to stop urine flow during diuresis is about 70 mm. Hg (Winton, 1937).

In experiments with anesthetized dogs, it has long been known that the kidney swells during diuresis (Winton, 1937). Brodie (1914) states that it may increase 30 per cent in size. Furthermore he reports that the tubules are greatly dilated. With dilation, the intratubular pressure would also presumably rise, and this has, in fact, been observed qualitatively by Walker and Oliver (1941) when cannulating renal tubules with a micropipette. Because the lumen of each tubule becomes greater, but usually not its outside diameter, Brodie reasons that each tubule increases in length and that this is responsible for the swelling in total renal size. It is the total swelling which we are indirectly measuring with the present technique; one would expect the swollen kidney to have a high interstitial pressure. The IRP does not, however, increase during diuresis in the unanesthetized dog. We may therefore deduce that the kidney in this circumstance is not inflated with urine and does not swell.

We have shown that the kidney is inflated with blood, the inflating pressure being contributed by the cardiac pump (Swann, Moore and Montgomery, 1952; Swann, 1952). The present experiment, along with Brodie's experiment, shows that it may also be inflated with glomerular filtrate and urine. In connection with these inflations, the question arises: why does not the inflating fluid, be it blood or glomerular filtrate, drain off at once? What holds it back from running out the appropriate effluent? In the case of the blood inflation, we have shown that there is a sudden pressure drop in the vascular system just at the arcuate-interlobar junction of the renal veins (Swann, Hink, Koester, Moore and Prine, 1952). Presumably, therefore, a strong resistance—perhaps a constriction—will be found at this junction; we already suspect that it is similar in structure to the resistance that appears to reside in the vortex veins of the eye (Swann, 1952). The same course of reasoning must be applied to the renal tubular system: in the normal kidney, the intrarenal pressure would collapse the tubules unless intratubular pressure exceeds IRP. Since intrapelvic pressure is close to zero (Lucas, 1908), the pressure in the tubular system must drop from 25 mm. Hg to about zero at some point above the epithelial lining of the pelvis. In the case of the diuretic (anesthetized) kidney, the pressure must drop from 55 to zero at some point. Where this point is or what its morphology is we do not yet know.

The difference between anesthetized and unanesthetized dogs in this reaction is still difficult for us to explain. It is not due to ureteral cramp or constriction, because in many of the experiments with anesthetized dogs, a ureteral catheter reaching into the renal pelvis, rather than a ureteral cannula, was employed. Even with this technique high IRPs were observed. The difference might be related to the oliguria that is so characteristic of deep anesthesia (Smith, 1951). But there are two drawbacks to this interpretation. First, an afferent arteriolar resistance is apparently responsible for some of the oliguria of anesthetized dogs (Smith, 1951). This should result in a low IRP, just as does epinephrine injection (Swann, 1952a). But the IRP during anesthesia is not low: it is 26 mm. Hg, compared with 25 mm. for unanesthetized dogs (Montgomery, Davis, Prine and Swann, 1950). Secondly, pituitrin antidiuresis is responsible for some of the oliguria of anesthetized dogs, as shown by de Bodo and Prescott (1945). But this type of antidiuresis has no effect on IRP, as shown experimentally above. For these two reasons, the recognized oliguria of anesthesia does not appear related to the genesis of the high IRPs here reported.

At present, we suspect that the constriction in the tubular system, which has been postulated above, is, for some unknown reason, stronger during diuresis of anesthetized animals. It would not be strong enough to hinder slow urine flows, but would, during anesthesia, be strong enough to hinder profuse urine flows. As table 1 shows, the highest IRPs were observed when urine flows were medium, not high; the postulated constriction, therefore, probably prevented the anesthetized dogs from experiencing the profuse urine flows which were observed in dogs without anesthesia. In the later, the urine can readily escape, but during anesthesia the urine cannot readily escape, and hence the kidney is inflated and the IRP increases.*

The present experiment is of considerable interest when considering the dynamics of flow of glomerular filtrate through the kidney. What forces cause flow down the tubule? This has always been a thorny problem. Winton (1937) suggests that modern theories of renal function demand a pressure head of 125–180 mm. Hg in Bowman's capsule to force fluid down the tubule and out the papilla. This borders on the absurd; it is, as Winton points out, due to our ignorance of renal physiology.* In the present experiment with anesthetized dogs, the intrarenal pressure rose to about 55 mm. Hg, accompanying the tubular inflation. This pressure was, we believe, caused ultimately by the blood pressure (that is by hydrostatic pressure from the heart), since without blood pressure, no urine would be formed to inflate the tubules. If to 55 mm. Hg we now add a plasma protein osmotic pressure of 25 mm. Hg, the pressure that the heart must furnish, in order for these diuretic kidneys to excrete urine, is about 80 mm. Hg. But this, of course, is close to the diastolic blood pressure—we have already used up, as it were, most of the available pressure from the cardiac pump, and there is very little left over to drive the glomerular filtrate down the tubule. The implication is that flow of glomerular fluid from capsule to papilla has, in these diuretic dogs, only an exceedingly small frictional resistance. Undoubtedly the process of re-absorption draws fluid down the tubules somewhat and thus aids fluid movement. But during diuresis the main resistance to flow appears to be the intratubular pressure. Glomerular filtrate, then, dilates the tubules strongly; and once this is done, the filtrate apparently flows down the tubule with only a minimal propulsive force.

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* It should be noted that only one kidney was secreting urine in the anesthetized animals, whereas in the unanesthetized animals—unilaterally nephrectomized as they were—the single kidney left had compensated so that it was roughly equal to two kidneys (Moustgaard, 1949). This fact considerably confuses the interpretation offered above.

CONCLUSIONS

Profuse diuresis in pentobarbitalized dogs, induced by intravenous glucose, urea, sodium sulfate or saline, causes an abrupt rise in the intrarenal pressure from the normal of 25 mm. Hg to about 55 mm. This rise usually precedes the maximum urine flow and subsides before the diuresis stops. The diuresis also causes a rise of similar magnitude in the renal arcuate venous pressure. The response of unanesthetized dogs to diuresis is in sharp contrast: glucose, urea, saline or water diuresis caused only insignificant rises in intrarenal pressure. Pituitrin antidiuresis also was not accompanied with significant change in intrarenal pressure in the unanesthetized dogs.

The inflation of the kidney with glomerular filtrate and urine, which was indirectly measured in these experiments on diuresis, is discussed, as is the flow of glomerular filtrate down the tubule.

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* Zinsser (1951) has recently postulated that the glomerulus is a coupled elastic ram, capable of generating very high pressures. Such an action, however, is not necessary for urine flow, since kidneys form urine even though the blood pressure is steady and not pulsatile (Goodyer and Glenn, 1951).

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RENAL ARTERIOGRAPHY: REPORT OF A PERCUTANEOUS METHOD USING THE FEMORAL ARTERY APPROACH AND A DISPOSABLE CATHETER

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Renal arteriography appears to be of definite diagnostic value but has never been very popular.[1, 2, 3] The translumbar technique described by dos Santos, Lamas and Pereira Caldas in 1929[4] has been eminently satisfactory in some hands and has been used many hundreds of times.[2, 5] Although complications are frequent in animals[6] this is not the case in humans.[2, 7] The technique, however, is a rigid one: careful and restricted patient placement is necessary, once the needle is inserted the locus of dye injection cannot be varied, initial roentgenograms may not be satisfactory, and repeated pictures are frequently not possible.

In 1941, Farinas experimented briefly with a catheter method using a femoral artery "cut down."[8] He soon abandoned this in favor of injecting the dye at high speed through a femoral artery canula against the current of blood[9] as described earlier by Castellanos and Pereiras.[10] This "counter-current" method has been improved by Freeman et al.[11] but cannot be seriously considered a satisfactory method of renal arteriography. The same may be said for attempts to adapt angiocardiography to renal study.[12] More recently, the femoral artery catheter method has been revived by Helmsworth, McGuire and Felson[13] who use a large bore polyethylene tube introduced by a "cut-down" and by Goodwin, Scardino

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and Scott[2] who pass their catheter by way of a branch of the deep femoral artery. These newer catheter methods are more versatile than the translumbar procedure but are unduly time consuming and perhaps dangerous.

It is the purpose of this paper to report a method of arteriography that is a real advance in simplicity, versatility, and probably in safety also. A large bore (12 or 14 gauge) hypodermic needle is introduced through the skin into the femoral artery. By way of this needle a polyethylene catheter is passed to the desired level in the abdominal aorta and roentgenograms are taken after simple hand injection of radiopaque medium with an ordinary syringe. Repeated pictures may be taken with the catheter tip and patient repositioned as desired. It is possible, for instance, to prevent the often confusing injection of the celiac axis. Only local anesthesia is used and haste is unnecessary at any stage. A single physician is required, and since at completion only a needle puncture remains there is almost no morbidity. Roentgenograms obtained are technically very satisfactory and there have been few failures or complications in our hands in 26 cases. This method was first used in dogs in 1947[14] and in humans in 1949.[15]

TABLE 1. *Specifications of polyethylene catheters* for abdominal arteriography.*

ARBITRARY DESIGNATION	SIZE	CONDUCTING NEEDLE†	HUB NEEDLE‡	[illegible]
13 gauge	Inside diameter 0.047 in. Outside diameter 0.067 in. Length 24 inches	13 gauge or 14 gauge special§	18 gauge	49 wire gauge
12 gauge	Inside diameter 0.055 in. Outside diameter 0.075 in Length 24 inches	12 gauge or 13 gauge special§	17 gauge	47 wire gauge

* Clay Adams. Co., sterilized by immersion in 1:1000 zephiran hydrochloride for 18 hours. The ends are cut on the bias.

† Standard 2 inch, short bevel.

‡ Blunted to avoid piercing the catheter.

§ Two inch, T 462 LNR, Becton, Dickinson and Co.

MATERIALS AND METHOD

The technique is described in detail because it is an exacting procedure. Specifications of the various arterial catheters are given in table 1. The larger catheter is recommended except in small or thin individuals. The patient is prepared as for an excretory urogram. Mild analgesia with morphine sulphate is recommended.

It is our practice to insert the catheter before the patient is taken to the x-ray department. The thigh is abducted, the groin shaved, prepared aseptically, and draped with towels. The tissue over the upper femoral artery is infiltrated with a local anesthetic agent not containing a vasoconstrictor. A disposable polyethylene catheter is carefully inspected for kinks and discarded if any are found. The catheter is fitted with a blunt needle (table 1) filled with dilute heparin in isotonic saline, and closed with a needle plug (Becton, Dickinson and Co. 417 A). The free beveled catheter end is passed through the stopcock and large needle to check their size and then withdrawn (fig. 1). A syringe half filled with heparin-saline is attached to the stopcock-needle combination and the needle is then advanced squarely into the femoral artery, guided by its pulsations. It is easy to miss the artery during the insertion but accurate aim denoted by feeling the arterial pulsation directly transmitted to the needle will generally avoid this. It is better to have the needle bevel cut the artery longitudinally rather than transversely, as less bleeding results. Care is taken not to withdraw the needle once it has entered the artery, since replacement may be made difficult by blood leakage.

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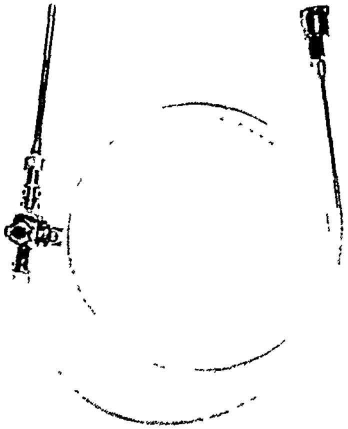

FIG. 1. Equipment for renal arteriography consists of 12 or 14 gauge needle, specially drilled stopcock, 24 inches of polyethylene catheter, blunt needle and needle plug. By courtesy of *Surgery, Gynecology and Obstetrics.*

Unless blood pushes vigorously into the syringe, the needle is not in the proper position. After correct needle placement, the stopcock is closed and the syringe removed. The catheter is started into the stopcock; this is then opened and the catheter is slowly pushed into the artery for a distance of about 6 to 12 inches. When resistance at the needle tip is encountered the catheter is never forced as this may kink the tubing rendering it impossible to pass. If kinking occurs the catheter is replaced with a new one. It may be withdrawn into the needle and the latter moved slightly if an attempt to insert the catheter is not successful. Generally some practice is required before catheterization is carried out easily. When the polyethylene tube is properly placed, the neede is withdrawn, pressure being applied for several minutes over the site of puncture to prevent bleeding. Persistent slow bleeding may rarely require continued pressure during the remainder of the examination or during manipulation. The tube is clamped with a rubber-shod hemostat, the blunt needle removed, the large needle and stopcock slid off the free catheter end, and the blunt needle reinserted. Final positioning is done after the needle is removed. By experience we have found that if there is about 10 inches of catheter remaining outside, the intraarterial end will be in the proper position. This distance can be measured on the leg before the percutaneous catheter insertion to facilitate reaching the proper position. It is better to have too much catheter in the artery than too little, since partial withdrawal is very simple. A small sterile dressing is applied and the catheter securely taped to the patient's skin. The catheter is kept filled with dilute heparin saline; a continuous drip is not necessary.

Approximately 20 cc of 70 per cent diodrast is used for aortography but good pictures can be secured with as little as 10 cc. This is placed in a regular 20 cc syringe and injected by hand over a period of three to five seconds, while the patient is performing the Valsalva maneuver,* the exposure being made just before the end of injection. The patient is warned that he will experience some pain or burning during the injection and a feeling of warmth immediately afterwards, followed sometimes by fleeting pains in the lumbar region and rectum. The position of the catheter is always checked by a roentgenogram immediately before diodrast is given (fig. 2). The diodrast used for positioning the catheter serves

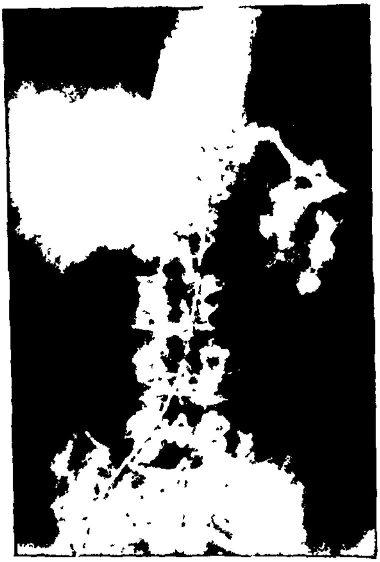

FIG. 2. Catheter has been filled with 70 per cent diodrast and small puff of diodrast is seen at tip between first and second lumbar vertebrae. This is suitable location for preliminary film but tip will probably need to be located somewhat lower for pure renal injection. 12 gauge catheter.

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* Five to ten seconds after the patient begins a forced expiratory effort against a closed glottis, there is usually a blood pressure fall and a slowing of the circulation which makes a heavier dye concentration possible.[11]

for a sensitivity test. Potter-Bucky films at 1/10 second, hard enough for bone detail, are suitable for aortography. Serial films have occasionally been made using a rapid cassette changer to study different phases of filling of the renal circulation (fig. 3).

Withdrawal of the catheter after use usually results in momentary brisk bleeding and requires one precaution, firm continuous pressure at the site of puncture for at least five minutes. The groin is then inspected and if no hematoma is forming and free bleeding has stopped, a small dressing is applied to remain for 24 hours. The patient is kept in bed for two to three hours after catheterization, following which he resumes his preoperative status.

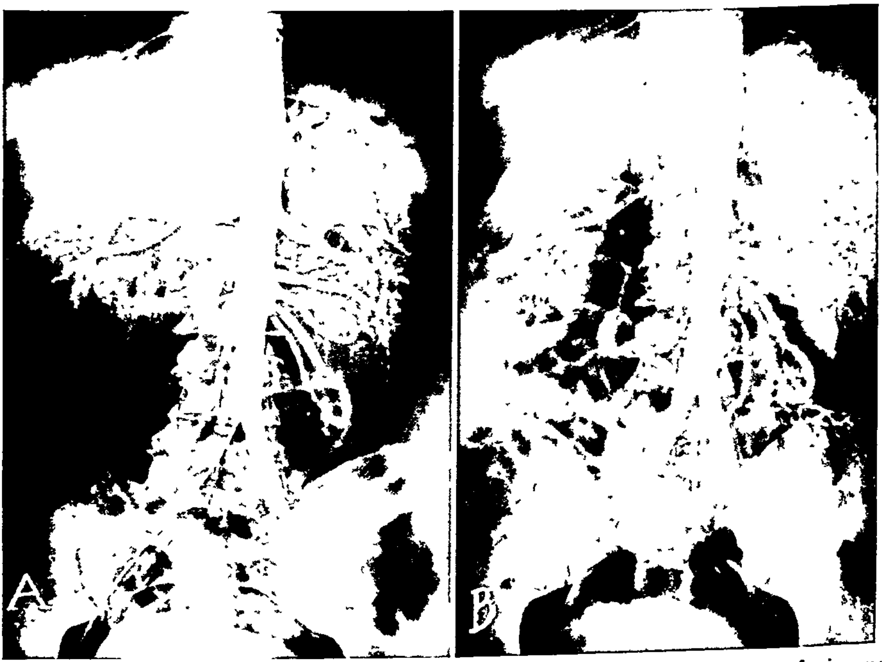

FIG. 3. Normal renal arteriogram in 28 year old white man. Somewhat confusing pattern on left because of injection of celiac axis. *A*, renal arteries alone are injected in this early film. *B*, somewhat later film shows delineation of entire parenchyma. 12 gauge catheter.

RESULTS

Examination of the abdominal aorta and its branches was undertaken in 26 patients, in most instances to obtain renal arteriograms. Satisfactory films were secured in 25. In one case the catheter was passed to the bifurcation of the aorta, but could not be advanced further and no film was made. In four instances, an initial attempt to pass a catheter failed but successful catheterization was carried out at a later date. We did not hesitate in occasional instances to use the opposite artery immediately if an initial attempt failed. In a number of cases films were a positive aid to diagnosis (fig. 5). It was possible to avoid confusing filling of the celiac axis when desired (fig. 4).

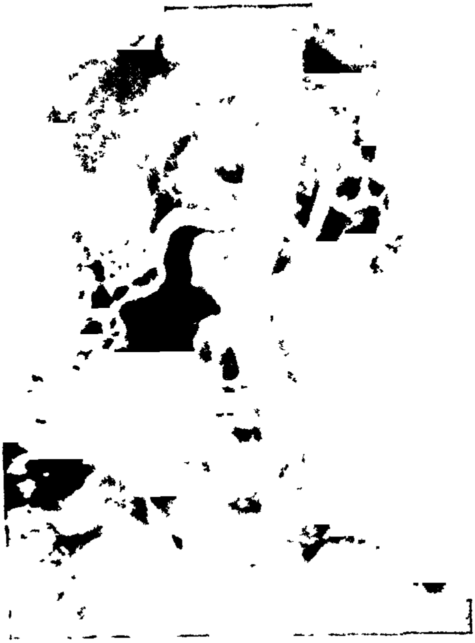

Fig. 4. Renal arteriogram in a 46 year old Negro hypertensive. Correct positioning of tip and rapid injection of dye are shown in this technically excellent film. Aortic tortuosity is result of marked hypertension. Some barium is present in colon. Diodrast (20 cc of 70 per cent) and 12 gauge catheter were used. By courtesy of *Surgery, Gynecology and Obstetrics*.

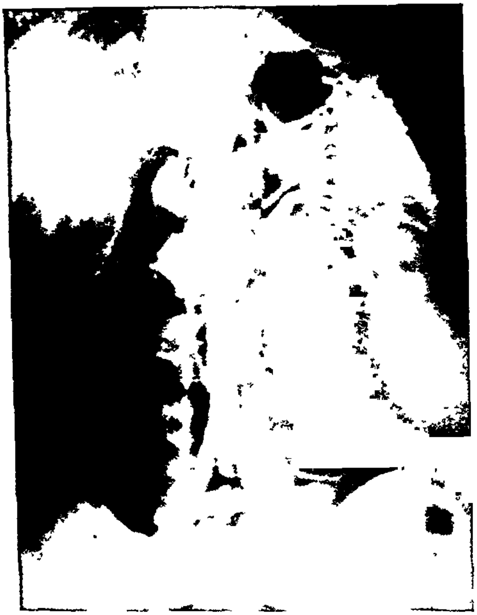

Fig. 5. Arteriogram in a 20 year old white man. Renal studies were undertaken because of mild hypertension and right costovertebral angle pain. Excretory urography failed to delineate right kidney and no right ureteral orifice was seen on cystoscopy. Renal arteriogram indicates absence of right kidney. Hepatic, splenic, mesenteric and adrenal arteries are very well shown. 12 gauge catheter was inserted by way of left femoral artery.

Arteriography was generally completed in 45 minutes to 2 hours but on a few occasions was more prolonged. The procedure, always completed without general anesthesia, was essentially painless except for brief discomfort following the diodrast injection. This was seldom enough to prevent repeated injections. Nausea and vomiting were infrequent. With the exception of two of the three patients noted below, ambulation was allowed within two to three hours. The minor ecchymoses occasionally noted were almost without discomfort.

Significant reactions occurred but three times. One patient became hysterical following a diodrast injection and brief psychiatric treatment became necessary. A second patient developed an arteriovenous fistula between the femoral artery and a branch of the saphenous vein. This was noted 27 days after catheterization and was repaired under local anesthesia. The third patient had an abrupt fall in blood pressure following injection of 20 cc 70 per cent diodrast although the test injection had been without noticeable effect. The situation was at no time serious and pressure was restored to normal levels with several small injections of adrenalin.

DISCUSSION

Advantages of percutaneous arterial catheterization. Percutaneous insertion appears to be a safer and simpler method of introducing a catheter into a large artery than surgical "cut-down" and no thromboses, infections, or secondary hemorrhages occurred in our hands. The equipment required for the procedure is simple and inexpensive. A thin walled polyethylene catheter has an adequate volume flow for contrast arteriography when hand injected diodrast is used. No special injecting apparatus need be employed. The single physician performing the procedure may be protected from radiation exposure by being at a distance from the x-ray field. Since dye is injected against the blood current, thereby slowing it, only small volumes of contrast medium need be used and repeated pictures may be secured safely in different positions in the unanesthetized patient. The percutaneous method of arterial catheterization is also adaptable to intra-arterial transfusion and direct arterial pressure studies.

Disadvantages of percutaneous arterial catheterization. The disadvantages of the percutaneous catheter technique for abdominal arteriography are not many. A considerable degree of skill is necessary to pass the catheters and occasionally this is not possible. The vessels may be deformed so that passage of the catheter is arrested and arteriography cannot be carried out at the optimum level. The position of the catheter tip must be absolutely identified by a check film. Some practice is required in injecting dye since this must be done as rapidly as possible if excellent films are to be obtained. Unless proper care is exercised throughout the procedure, sizable hematomas may easily result. If surgery is contemplated soon after the procedure it is advisable, if possible, to perform the arteriogram on the opposite side because of occasional iliac tissue discoloration.

Possible complications of percutaneous arterial catheterization. Hemorrhage and hematoma formation: A palpable swelling was relatively infrequent but discoloration of skin was present in many. Discoloration of the iliac region was noted once at operation.

Kinking of catheter during insertion: This occurs when passing the catheter against resistance or a deformed vessel. Usually it necessitates using another catheter, but is easily avoided with proper technique.

Shearing of the catheter: This is a possible danger with inexpert handling of the catheter but has not occurred in any of our cases.

Thrombosis of the femoral artery: Arterial spasm of several hours' duration simulating thrombosis has been noted several times but no thromboses have occurred. Thromboses have been reported with "cut-downs" on the femoral artery.[11]

Arterial rupture from catheter tip: This has been reported by Goodwin, Scardino and Scott using a heavy ureteral catheter[7] but none have occurred in our series. Injection should never be done until the catheter tip is in the aorta or iliac artery.

Danger of opaque media injection: Hypersensitivity reactions to diodrast occur occasionally and sometimes result in death.[16] We noted one episode of hypotension easily treated with adrenalin. Patients should be tested for sensitivity and the usual drugs to combat reactions should be available.

Formation of an arteriovenous fistula: This unusual complication resulted once, and must be considered most unlikely.

SUMMARY

A simple and versatile method of renal arteriography is reported. Contrast medium is injected into a polyethylene catheter inserted percutaneously by way of a femoral artery to the required aortic level. Successful abdominal aortagrams have been carried out in 25 cases. Failures and complications have been infrequent. The roentgen films obtained are frequently superior to those obtained by better known techniques.

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PERIDURAL ANESTHESIA

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In the vertebral canal the spinal nerves can be blocked either by introducing the medication inside or outside the dural sac. Referring to the former, we have what is called "spinal anesthesia," in which the spinal nerves are blocked within the subarachnoid space (intrathecal injection). In the latter course, we have a "peridural anesthesia" and the spinal nerves are blocked outside the "dura," by the injection of the anesthetic solution into the peridural space. Therefore, we shall consider "peridural" any anesthesia which is based on the administration of an anesthetic in any point of the peridural space, using any technique, for they all are founded on the same principle.

Depending on the route and technique used for the injection, different names have been applied to peridural anesthesia, as for instance: caudal block or epidural anesthesia, sacral block (Pitkin), transsacral block, peridural segmental anesthesia (Dogliotti), high epidural anesthesia (Krönig, Lundy), continuous caudal anesthesia and continuous peridural block.

Peridural anesthesia was probably first done by Corning (1885), when he made injections of anesthetics between the spinous processes and produced anesthesia. In 1901, Cathelin and Sicard used to inject medication in the sacral peridural space for treating urinary incontinence, and also neuralgias affecting the lower half of the trunk.

Stoeckel, in 1909, reported the use of caudal block with a single injection of procaine (novocain) in 141 normal deliveries. Although the results were not uniform, some relief in pain was observed in 80 per cent of these patients.

Caudal block was first used in surgery in 1910, by Läwen. He did not consider it practical until he learned of Gros' discovery that the action of procaine is potentiated by the addition of sodium bicarbonate. After him, many surgeons used this method with good results for operations in the perineum, genitalia, and also for obstetrical purposes (Schlimpert and Schneider).

Krönig, Schlimpert and Schneider attempted to extend the field of caudal anesthesia by using a forced Trendelenburg position and injecting larger amounts of anesthetic in a greater concentration. They called this procedure "high epidural anesthesia." They were able to obtain a complete anesthesia up to the eighth dorsal segment 30 minutes after placing the patient in Trendelenburg. However, the results were not uniform as proved by the fact that in 93 high epidurals, general anesthesia had to be resorted to in 53 instances, even though an amount of up to 800 mg. of novocain (procaine) had been used, plus strong sedation (morphine, scopolamine and sodium luminal combined).

Until 1920, the only route used for blocking the spinal nerves outside the "dural sac" was through the sacral hiatus, with the only exception of Corning's work. In this year, Fidel Pagés reported on the possibility of obtaining anesthesia of the chest or abdomen by puncturing the peridural space in the thoracic or lumbar regions and injecting an anesthetic solution at that level. He used this anesthesia 43 times. At first he used a 1 per cent solution of novocain with very satisfactory results, but soon found the 2 per cent solution to work even better.

In 1927, Heldt and Moloney reported that the peridural space could be precisely located by a negative pressure which they accidentally found to exist on it. No suggestions on the use of this discovery on peridural anesthesia were made.

Only in 1931 was peridural anesthesia revived; this time by Dogliotti, an Italian surgeon. He reported before the Italian Surgical Congress on what he thought to be a new type of anesthesia, which he called "segmental peridural anesthesia" and described his original technique for peridural tap, based on the "lessened resistance" to injection encountered on the peridural space. One year later, A. Guitierrez, from Buenos Aires, described a new sign used on the location of the peridural space—the so called "sign of the drop."

TABLE 1. *Anesthesias used in 134 major operations done between March 1, 1948 and February 15, 1949*

				TOTAL	% OF TOTAL
Segmental Peridural	Alone	49	36.1	70	51.7%
	Plus i.v. penthotal	14	10.4%		
Epidural	Alone	6	4.4%		
	Plus i.v. penthotal	1	0.8%		
Spinal	Alone	39	29.3%	44	32.9%
	Plus i.v. penthotal	5	3.6%		
General	Adults	11	8.4%	17	12.8%
	Children	6	4.4%		
Local		3	2.6%	3	2.6%

From that time, the procedure has been widely used by many surgeons in Europe, South and North Americas. Many variations in technical details have been described; new instruments for its performance have been devised, and new anesthetics have been synthetized. All these make peridural anesthesia one of the best methods of anesthesia that the surgeon has in his hands, because of its safety and very satisfactory results.

Ever since 1934, when Dr. J. Silva de Assis returned from Germany, where he learned the Dogliotti technique, at von Lichtenberg's clinic, peridural has been the routine anesthesia in both his private and ward practice. In 1939 he reported on 300 cases. From then on, over 700 more cases have been done, with the total, so far, amounting to over 1,000 cases. Most of our patients fall into the urological group, but we have also used peridural in nonurological cases. The results have been very satisfactory. In our series, only 2 fatal accidents occurred; both in cases where the anesthesia had been given by a young surgeon, rather inexperienced in its technique. They were both due to massive injection

TABLE 2. *Summary of 134 major operations with the anesthesias used*

	OPERATION	ANESTHESIA				
		Peridural	Epidural	General	Spinal	Local
Kidney and kidney pelvis	Denervation of renal pedicle	7	0	3	0	0
	Nephrectomy	14	0	3	0	0
	Polycystic kidney (Goldstein)	1	0	0	0	0
	Plastic on kidney pelvis	0	0	1	0	0
	Pyelolithotomy	3	0	1	0	0
Bladder	S.P. cystostomy	2	0	1	12	2
	Cystolithotomy	1	0	3	2	0
	Diverticulectomy	1	0	0	0	0
	S.P. resection of internal sphincter	1	0	1	0	0
	S.P. electrocoagulation and biopsy	1	0	0	0	0
	Transurethral biopsy	0	2	0	4	0
Ureter	Ureterocystoneostomy	2	0	0	0	0
	Intubated ureterotomy	1	0	0	0	0
Prostate	Transurethral resection	0	2	1	13	0
	Retropubic prostatectomy	14	0	0	0	0
	Suprapubic prostatectomy	2	0	0	1	0
	Radical perineal prostatectomy	0	1	0	1	0
Seminal vesicles	Seminal vesiculectomy	3	0	0	0	0
Urethra	Cure of urethrocutaneous fistula	0	0	0	1	0
	Perineal urethrostomy	0	0	0	2*	0
	I & D of peri-urethral abscess	0	0	0	1†	0
	Plastic on hypospadias	0	0	0	1*	0
Penis	Amputation of penis	1‡	0	0	0	0
Epididymis	Bilateral epididymectomy	0	0	0	1	0
Miscellaneous	Total cystectomy with bilateral ureterosigmoidostomy	2	0	0	0	0
	Orchidopexy and herniorraphy	2	0	1	1	0
	Herniorraphy alone	1	0	0	0	0
	Bilateral ureterosigmoidostomy alone	1	0	1	0	0
	Colostomy	0	0	0	1	1

TABLE 2.—*Continued*

	OPERATION	ANESTHESIA				
		Peridural	Epidural	General	Spinal	Local
Miscellaneous— *Continued*	Entero-enterostomy	2	0	0	0	0
	Presacral neuronectomy	0	0	1	1	0
	Cure of vesicovaginal fistula	1 (S.P.)	2 (Vag.)	0	0	0
	T.U.R. bladder tumor	0	0	0	1	0
	T.U.R. ureterocele	0 .	0	0	1	0

* Most of these cases are not listed but were done under general anesthesia because of the age.

† Most of them done under spinal at the same sitting the S.P. cystostomy was done.

‡ Most of them not listed here but done under anesthesia of the corpora cavernosa.

S.P. = Suprapubic approach.

Vag. = Vaginal approach.

in the subarachnoid space, as proved by pharmacological analysis of the spinal fluid on postmortem.

The greater danger of peridural consists of the mistaken injection of the entire dose of anesthetic intrathecally; this amount, being about ten times the average dose for spinal, will cause, when given intrathecally, a massive block, including the respiratory and circulatory centers, followed by death. For this reason, many surgeons, once very fond of peridural, have abandoned it after their first fatalities.

Notwithstanding our two fatalities, we still think that peridural is a very safe and dependable procedure as long as certain precautions are taken (see section on Technique).

For the best understanding of peridural anesthesia, it is well to know the following anatomical fundamentals of the peridural space.

ANATOMY

As in the cranial dura mater, we can consider the spinal dura mater as having two layers; an internal or meningeal layer, and an external or endosteal layer.

The external (endosteal) layer is very thin and blends itself with the periosteum, which lines the inner surface of the vertebral canal, and they are reinforced by the various ligaments of the spine—the ones interesting us most at the moment being the ligamenta flava. Superiorly, the endosteal and meningeal layers are fused, and adhere to the periosteum, which lines the circumference of the foramen magnum. Inferiorly, the endosteal layer extends to the second coccygeal vertebra, and fuses with its periosteum.

The inner lining (periosteum and endosteal layer of the dura) of the vertebral canal is continuous throughout, except laterally at the various intervertebral foramina, where it is interrupted to give passage to the spinal nerves.

This was known by the anatomists and also proved radiologically by Dogliotti. We also proved it by the injection of an anesthetic solution in the peridural space, adding to it either neo-iopax or diodrast, and making serial x-ray films. Using this technique, the radio-opaque substance was seen outside the vertebral canal shortly after the peridural injection (fig. 1).

The meningeal layer of the dura mater is the true spinal dura and is in close contact with the arachnoid, involving the spinal cord as a continuous and impervious sheath. Between the spinal cord and the meningeal layer of the dura, there are the subdural and subarachnoid spaces. Superiorly, as we said before, there is a complete fusion of this meningeal layer with the endosteal layer and the periosteum of the foramen magnum. Inferiorly, at the level of the second sacral vertebra, the true dura mater closely surrounds the filum terminale, thereby closing the subdural cavity, and descends to the back of the coccyx, where it blends with the endosteal layer.

The peridural space is situated between the two layers of the spinal dura mater. From our brief description, we can conclude that the only communication of the peridural space, with the structures outside the vertebral canal, is made through the intervertebral foramina, where the dura's endosteal layer is discontinued; at this level, the peridural space and paravertebral tissues are continuous. The peridural space is entirely isolated from the intracranial structures, since the two layers of the spinal dura blend with each other and are attached to the circumference of the foramen magnum.

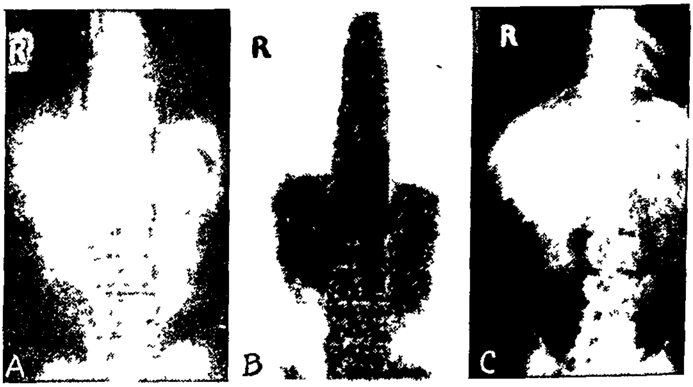

FIG. 1. *A*, case 1. Twenty minutes after injection. *B*, case 1. Forty minutes after injection. *C*, case 2. Thirty minutes after injection.

Another important point to be remembered. Although the spinal cord ends at the level of the second lumbar vertebra, the dural sac goes further down, ending at the level of the second sacral vertebra, with the fusion of the meningeal layer of the spinal dura mater to the filum terminale.

The peridural space contains a semi-liquid fat, loose areolar tissue, and the internal vertebral venous plexus. However, while the venous plexuses are more abundant laterally, the fat is more marked in the posterior midline.

The roots of the spinal nerves traverse the peridural space, going downward and outward in the direction of the intervertebral foramina, where they join and form the spinal nerves. The newly formed spinal nerves divide again into anterior and posterior branches. The anterior branches receive connections from the sympathetic chain (rami communicantes).

In their course through the peridural space, the nerve roots are surrounded by tubular prolongations of the meningeal layer of the dura, which go as far as the intervertebral foramina, and blend with the fibrous neuralemma and perineurium of the nerves.

Inside the peridural space, the spinal cord and its covering do not occupy the center. As a matter of fact, anteriorly, the peridural space is a potential space—the two layers of the spinal dura mater being in close apposition. Most of the peridural space (nine-tenths) lies laterally and posteriorly; the size of it varies with the region, however. The distance between the two layers of the dura averages between 3 and 6 mm. posteriorly. At the level of the second lumbar vertebra, the peridural space occupies about one half of the vertebral canal.

The distance between the skin and the peridural space varies with the region considered, and also with the individual. The sacral peridural space is very superficial; in the lumbar and dorsal regions it is deepest. In some individuals, when performing a peridural tap at the lumbar region, the space is punctured after introducing the needle for 2.5 to 3 cm., while in others it has to be inserted for 8 or 9 cm. However, we can say that the average distance varies between 4 and 6 cm. at the lumbar or dorsal regions.

The peridural space just described, may be entered at any point along the vertebral canal. In this paper, we are mostly concerned with the segmental peridural anesthesia (Dogliotti), and the caudal or epidural anesthesia.

The first technique uses the cervical, dorsal, or lumbar peridural space, and the second one, the sacral canal (sacral peridural space or epidural space) for the anesthetic injection.

Once a solution is injected in the peridural space, no matter at which level, it spreads both upwards and caudally to a distance proportional to its amount and the speed of injection.

The solution, however, never goes any higher than the foramen magnum, because that is the superior limit of the peridural space—therefore, no danger of contact between the anesthetic and the spinal bulb.

Besides, the solution leaves the peridural space through the intervertebral foramina and spreads to the paravertebral tissues. Dogliotti had demonstrated this by doing serial x-rays in cadavers after injecting lipiodol in the peridural space. Lipiodol could be seen leaving the peridural space at the end of 20 minutes, but this feature was more striking at the end of 6 hours.

However, Dogliotti's experiment was not too convincing, since he used an oily substance in a cadaver and in a small amount (20 cc at the most), whereas peridural anesthesia is done with watery solutions injected in large amounts (up to 50 cc).

In an attempt to see the final destination of solutions, we injected peridurally an anesthetic solution to which we previously added neo-iopax or diodrast, using the same technique as for peridural anesthesia. This investigation was carried out twice, and we present a summary of the 2 cases.

Case 1: F. C. C., 50 year old Negro. Puncture: Between L2 and L3. Solution: Procaine 450 mg. plus 10 cc diodrast plus 22 cc saline. Position: Left lateral decubitus. Injection: 5 cc immediately after puncture; 10 cc 7 minutes after puncture; 17 cc 11 minutes after puncture. Total dose: 32 cc (average volume used on our peridurals).

The patient was kept in the left lateral decubitus for 20 minutes after the puncture. At 15, 20, 40, and 105 minutes after the initial dose, x-ray pictures were made (fig. 1, *A* and *B*). Anesthesia was checked at 20, 40, and 105 minutes.

Our first film (15 minutes) revealed that the solution spread upwards as far as we could see (D 7), and downwards to L2; besides, the diodrast could be seen outside the spinal column in the same levels as inside and extending horizontally to a distance of about two centimeters to the left. On the right side, some diodrast was seen leaving the intervertebral foramen between D12 and L1. At the end of 20 minutes, the patient was turned flat on his back, where he remained until the end of the experiment. Another picture was made and the level of anesthesia was checked. The x-ray showed the same findings as the preceding one, except for the fact that on the right side there was a concentration of the diodrast along what seemed to be the psoas border and also along the margins of the spinal column (fig. 1, *A*). At the same time, there was complete anesthesia of the left side of the abdomen, extending from the lower ribs to the inguinal region.

Forty minutes after the first injection, another picture was made; no dye was seen along the psoas border on the right, but diodrast was still encountered both inside and outside the peridural space—mostly on the left side (fig. 1, *B*). The patient had his abdomen anesthesized on both sides, from the lower ribs to the inguinal regions. At the end of 1 hour and 45 minutes, the last picture was made showing the pyelogram of the right kidney and dye still both inside and outside the vertebral canal. The anesthesia was subsiding at this time.

Case 2: M. R. J., 21 year old Negress. Puncture: Between L3 and L4. Solution: Procaine 450 mg. plus 20 cc neo-iopax plus 10 cc saline. Position and technique of injection: Same as in the first case.

X-ray pictures were made at the end of 15, 30, and 45 minutes. At the end of 20 minutes, there was complete anesthesia of the left side of the abdomen, extending from the lower ribs to the inguinal region; no anesthesia on the right side of the abdomen at any time (patient kept on the left lateral decubitus for 20 minutes after the first injection).

The x-ray findings were essentially the same as of the first case, with the difference being that dye spread more caudally, and a great amount of it was seen leaving the intervertebral foramina between L5 and S1 in the first film. Dye was also seen leaving the peridural space through all the intervertebral foramina in the lumbar and dorsal spines, chiefly on the left (fig. 1, *C*). Bilateral pyelograms were seen on the 30 and 40 minute pictures. Recovery of sensation took place at the end of 45 minutes; however, a great deal of dye was present in the peridural space and outside also at this time.

These findings are very important and helpful in explaining the location of the nerve block. At first, it is surprising how quickly a solution introduced into the peridural space spreads upwards, downwards, and at the same time, towards the paravertebral tissues. We were able to visualize dye in the paravertebral space in the first x-ray, made just after the last dose was given.

As said before under the heading of "anatomy," inside the peridural space, the nerve roots are covered by finger-like projections of the meningeal layer of the dura; these projections extend as far as, or beyond, the intervertebral foramina. This meningeal layer is impervious to anesthetics, as demonstrated long ago by Cathelin. Therefore, the nerve block in peridural anesthesia cannot take place either intrathecally or intraperidurally. It must take place in the paravertebral tissues, because only after leaving the intervertebral formaina do the nerve roots loose their dural coverings—therefore becoming pervious to anesthetics. Dogliotti had considered the possibility of this and of the nerve block inside the peridural space also. Pitkin claims that the block takes place "at the point where the covering becomes permeable—either in the peridural space or paravertebrally."

We have demonstrated radiologically how quickly a solution injected peridurally is found in the paravertebral tissues. This proves that the possibility of a paravertebral block is sound, and considering the aforementioned anatomical facts, we fully agree with Odom and also Harger et al., who do not admit the intraperidural nerve block.

PHYSIOLOGY

The anesthetic action is first noted in the sensory roots. The motor roots are affected shortly after the sensory, and are not affected as deeply as the sensory ones; this fact being explained only by admitting "a selective action of the anesthetics upon the sensory fibers." However, there is always good muscular relaxation with peridural—"no doubt due to the interruption of the nerve reflex at one point of its sensory pathway." Upon direct stimulation, the muscles very often show strong contractions.

The sympathetic fibers are also affected (rami communicantes and paravertebral sympathetic chain and ganglia); this makes possible intra-abdominal operations, with hard pulling on intraperitoneal organs with no disagreeable sensations to the patient and no harm to his condition. However, it has its effects on the blood pressure, for the vasodilation the sympathetic paralysis causes.

The fall in blood pressure, so marked in spinal anesthesia, is caused by both the block of sympathetic nerves and also the impaired venous return (which is due to the paralysis of voluntary muscles—thereby decreasing the muscle pump-action—and also the insufficient respiration). In the peridural anesthesia, the venous return is very little affected, because the voluntary muscles paralyzed are few and the respiration is not affected at all. Therefore, we have only the sympathetic anesthesia to account for the drop in blood pressure.

A fall in blood pressure has occurred in most of our cases, while the first reports on peridural anesthesia claimed the pressure suffered no change. I believe this is due to the fact that we inject the total amount in much less time, producing sympathetic paralysis so rapidly that the compensating factors do not have time to act. However, giving, with the premedication, some vasopressor substance (such as ephedrin sulphate, 25 mg.), we can save a lot of time with no danger to the patient's well being.

SIDE EFFECTS OF PERIDURAL ANESTHESIA

We said before that the blood pressure suffers a slight drop, which is easily controllable by medication (intravenous fluids and vasopressors). Vomiting very seldom occurs, either during or after the operation.

The sensation of "dead limbs," that worries some patients so much during spinal anesthesia and makes them very apprehensive, is not present; the patients can feel and move their legs at will, and therefore co-operate with the surgeon.

The respiration is not usually affected, since the motor paralysis is not complete.

Postoperative headaches are not encountered in this type of anesthesia. However, we have seen cases of adynamic ileus.

DRUGS

Any drug suited for local anesthesia can be used for peridural block. In our periduals, we use mostly pontocaine (also called tetracaine (Winthrop) and pantocaine (Bayer) in the 1:500 (0.2 per cent) strength. We have also used intracaine hydrochloride (2 per cent) and procaine (or novocain, 1.5–2 per cent). From March 1948, until February 1949, we have used peridural anesthesia 70 times: intracaine was used once; procaine, 3 times; and pontocaine 66 times (46 times with pantocaine [Bayer] and 20 times with tetracaine [Winthrop]).

Our solutions are freshly made by dissolving the tablets or the powder in sterile saline (hypotonic solutions cause marked pain when injected peridurally). We do so because we believe that the drugs lose their potency when kept for a long time in solution. Usually we make 50 cc and add to it epinephrine (10 drops to each 50 cc). We have had very good results with all the drugs just mentioned.

Nevertheless, there are times when the sensation of touch is not completely lost. In these cases, when the patient is not too co-operative, we have supplemented the peridural anesthesia with sodium penthotal intravenously (making a solution of 1 gm. sodium penthotal in 1 liter of 5 per cent glucose and giving it in the Murphy drip). As soon as the patient falls asleep, we start the operation and they never react or complain of anything, even though the dose is barely sufficient to produce sleep. In our 70 cases last year, we used this combination 15 times, with the most gratifying results.

The anesthesia with pontocaine usually starts 10–15 minutes after the final dose is given; with procaine or intracaine, it begins in a little less time and lasts from 1 to 1½ hours, whereas pontocaine lasts from 1½ to 6 hours. After the surgical period of anesthesia is over, there is still a period of analgesia, very variable in length, which makes the first postoperative hours very comfortable.

TECHNIQUE

For practical reasons, we will describe separately the technique for the puncture in the peridural (segmental peridural), and for the caudal anesthesia. Since the technique of injection and the precautions to be taken are the same in both procedures, they will be described together.

With either type of anesthesia, we use 100 mg. of demerol or 10 mg. of morphine as premedication; on the segmental perridurals, to compensate the fall in blood pressure, due to sympathetic block, we add 25 mg. of ephedrin sulphate to this. The premedication is given about 10 minutes before the tap, so that its action will start at approximately the same time the anesthesia begins (i.e., 20 minutes after the puncture). We consider the sedation very valuable in diminishing the patient's apprehension, that always precedes any operation.

The peridural tap may be done at any level of the cervical, dorsal, or lumbar spine, its height depending on the area of anesthesia desired. In short, we can say that the higher the area to be anesthetized, the higher the puncture should be. In our urological work, we use mostly the low dorsal or high lumbar puncture for operations above the level of the umbilicus (kidney and upper ureter), and a low lumbar puncture for operations below the umbilicus (lower ureter, bladder, prostate, genitalia and sigmoid).

The puncture is much easier to perform in the lumbar spine, because at that level the spinous processes do not overlap each other; also, the peridural space is wider. For this reason, many surgeons and anesthetists prefer the low lumbar puncture for any operation, taking advantage of the gravity to raise the level of anesthesia. We feel that by varying the level at which the needle is inserted, according to the area to be anesthetized, we can concentrate the anesthetic action on those nerve roots we want to block most. Therefore, the difficulties encountered are compensated by better results.

Abajian goes further and, considering the different level of sympathetic and voluntary nerve sources, advises two taps at different levels. When using this technique, much less anesthetic is needed to obtain an anesthesia of the same intensity and extent; but we have not used this technique, since we consider it doubles the anesthesia hazards and that the results are not any better than those secured with a single tap at the proper level.

The puncture can be performed with the patient sitting up and bending forward, or with the patient in a lateral decubitus with the back arched. In either case, a nurse should hold the patient in position. If the sitting position (the easiest one as far as the puncture is concerned) is employed, the patient can remain in this manner until the last dose is given, or the patient can be placed in lateral decubitus with the help of the operating room personnel immediately after the tap. We have abandoned the sitting method, because the anesthetic action tends to concentrate mainly on the lower segments if the sitting position is held until after completion of the injection in view of gravity. And to place the patient in lateral decubitus after the needle is inserted, increases the danger of puncturing the meningeal layer of the dura. Fainting spells also occur much more frequently with the sitting position.

The lateral decubitus gives much more comfort and safety to the patient, and we use this except when it is impossible to arch the back sufficiently to permit the introduction of the needle between the spinous processes properly. In this case, we utilize the sitting position for tapping, then immediately place the patient in lateral decubitus. In operations upon the flanks, we puncture with the patient lying on the corresponding side, and keep this decubitus for 20 minutes thereafter; this is intended to use gravity to divert most of the anesthetic solution towards the operative side.

Any type of spinal needle can be used for peridural tap, as long as it has a short bevel and an average caliber (No. 18 gauge). In our work, we use von Lichtenberg's "wing needle," because it gives a much better grip, which is essential for such a delicate procedure. The peridural space can be reached either by introducing the needle in the posterior midline between the spinous processes and pushing it straight forward, or by inserting the needle laterally to the midline, and pushing it forward and to the midline at the same time. Considering that the internal vertebral venous plexuses are more abundant laterally, we always do our punctures in the midline to avoid a bloody tap. Needless to say, before the peridural needle is inserted, the skin and subcutaneous tissues should be anesthetized in order to secure better co-operation from the patient.

Many methods of localizing the peridural space have been described. We can classify them as indirect and direct.

The indirect method is the simplest one and consists of withdrawing the needle, after an intrathecal tap, until no more spinal fluid is obtained. In spite of its simplicity, this procedure is not used any more, because of the frequent and serious accidents that follow its performance.

Everyone who has done many spinal taps has seen, more than once, a drop of spinal fluid, or more, leak through the needle hole in the skin upon withdrawing the needle. This is due to the fact that, once the meningeal dura is punctured, it takes some time for the hole to close—no doubt in view of its particular structure (fibrous and elastic tissue arranged in longitudinal parallel bands). By the same mechanism the spinal fluid leaks through this hole, an anesthetic solution injected into the peridural space, under pressure, will enter the subarachnoid space, and produce massive spinal anesthesia with all its bad consequences.

We are so strongly against this indirect method that, if in doing a peridural tap, the dura is accidentally punctured, we never try a puncture at another interspace for fear of an accident. Either we postpone the operation or use another type of anesthesia.

The peridural space can be localized directly; that is, without having to tap the subarachnoid space first and then withdraw the needle. There are many techniques for this purpose, but they all are based on one of the two following principles: 1) the negative pressure; 2) the lessened resistance.

1) Negative pressure: in 1927, Heldt and Moloney, while working on the cause of headaches that follow spinal anesthesia, accidentally found a negative pressure in the peridural space to exist. They discovered the value of this pressure to be between −1 and −18 mm. of mercury (true negative pressure), but they also demonstrated that if the needle is deepened a little more, thereby pushing the meningeal dura, the value of the negative pressure rises, sometimes until −30 mm. of mercury, before the dura is pierced (spurious negative pressure). The existence of this negative pressure is better explained by an increase in the capacity of the vertebral canal following the forced anterior flexion of the column; this negative pressure is soon compensated by a greater inflow of blood in the

internal vertebral venous plexuses. Therefore, it is wise not to bow the patient's back until the needle has reached the ligamentum flavum, in order to have a more marked negative pressure, which is very helpful if this particular method is used.

A. Gutierrez, of Buenos Aires, was the first one to use the negative pressure to localize the peridural space for anesthetic purposes. He devised a special needle with a concave hub, which could hold a drop of fluid. This drop, upon introduction of the needle in the peridural space, would be sucked. He called this "the sign of the drop."

According to his technique, after the vertebral interspace is chosen and the overlying skin anesthetized, his special needle is introduced as far as the interspinous ligament. The needle stylet is then removed and a drop of saline (or of the anesthetic solution) is placed in the needle hub in such a way as to hang from it. The patient's back is then arched and the needle gently pushed forward. Some resistance to the needle's progression is felt at first; that is, while it goes through the heavy ligamentum flavum. But, shortly afterwards, a release sensation is experienced, coinciding with the suction of the drop. This indicates the puncture of the peridural space, the negative pressure being responsible for the drop's aspiration.

Odom uses a common spinal needle and a special hollow glass indicator for the same purpose. The indicator is filled with sterile saline (a colored solution, such as methylene blue, may be substituted), and attached to the spinal needle after removal of the stylet. When the needle enters the peridural space, there is a fluctuation of the fluid in the indicator, varying from slight vibration to complete aspiration (depending on the value of the negative pressure).

A "U" manometer, connected to the spinal needle, can also be used for the purpose of detecting the peridural space negative pressure. As a matter of fact, this was the first device to be used (Heldt and Moloney, 1927).

2) The lessened resistance technique was first used by Dogliotti, and its performance is very simple. Once the patient is prepared and in position, the interspace is selected and the overlying skin anesthetized. A spinal needle (we use von Lichtenberg's wing needle) is inserted between the two spinal processes as far as the interspinous ligament. The needle stylet is withdrawn and a 10 or 20 cc syringe containing sterile saline is connected to the needle. The anesthetist then holds the needle with the left hand, and introduces the needle towards the vertebral canal, while pressing on the syringe's plunger with the right thumb. While the needle bevel is in the interspinous ligament or ligamentum flavum, it is very difficult to inject the saline and a resistance against the needle's progress is felt. But, as soon as these ligaments are passed, the plunger gives in with ease and a diminution of resistance to the needle's progression is noticed at the same time.

At this moment, the needle has entered the peridural space and the syringe is disconnected. A few drops of fluid usually flow from the needle; if the needle is in the peridural space, these drops are cold; if in the subarachnoid space, they will be warm (spinal fluid). Some anesthetists, feeling it difficult to perform the tap using the left hand to hold the needle, have modified this technique a little—the needle is held by both hands and the pressure on the plunger is maintained by a rubber band wrapped between the syringe tip and the plunger's finger rest. A finger cot inflated with sterile saline under pressure and tied over the needle hub can substitute for the syringe on the lessened resistance technique; the balloon so formed deflates itself when the peridural space is reached. In either case, both hands can be used for introducing the needle and the sensation of lessened resistance is visual; that is, the anesthetist sees the solution being delivered faster.

Some surgeons rely on the diminution of resistance to the needle progression in localizing the peridural space, but they also double-check it with the lessened resistance to injection.

We only use the lessened resistance technique for our peridurals, and believe it to be very dependable. Instead of using the rubber band or the finger cot modifications, we prefer to use the right hand for pressing the plunger. We believe that one more sensation is added if this technique is used, that being a tactile sensation of the plunger giving in with ease. The lessened resistance sensation never fails. Besides, the sudden injection of saline into the peridural space pushes the meningeal dura away from the needle—therefore diminishing the danger of its puncture. On the other hand, the negative pressure may be so little that one is unable to detect it; and the danger of puncturing the meningeal dura is always greater than when using the lessened resistance technique.

b) Epidural puncture: The use of epidural anesthesia (or caudal block) in urology is restricted to operations on the external genitalia, transurethral operations (such as transurethral resections and litholapaxy), operations on the perineum or by perineal approach (such as perineal prostatectomies), and in females when a vaginal route is planned. We use caudal block mostly for perineal prostatectomies and vaginal operations. The transurethral operations are better performed under spinal, because of the erections that very often follow epidural anesthesia. On the operations upon the male external genitalia, we more often use local anesthesias.

The epidural tap is very easy to perform; the sacral peridural space is very large and extends from the second sacral to the second coccygeal vertebra. Posteriorly and inferiorly, between the sacrococcygeal cornua, the bone protection of the peridural space is widely opened; this is the so-called sacral hiatus. The peridural space at that level is separated from the skin only by the superficial posterior sacrococcygeal ligament (of Cathelin). The sacral hiatus is the route used for epidural punctures. The standard technique for this purpose is as follows: The patient is placed in lateral decubitus with the trunk flexed anteriorly. The skin is prepared and the sacral hiatus located by palpation, and an intradermal anesthetic wheal is made at this site. Through this wheal a No. 18 or No. 20 spinal needle is inserted, perpendicular to the skin and so driven until a bony resistance is felt (the bone represents the anterior wall of the sacral canal). At this moment, the hub is directed caudally and at the same time the needle is pushed inside the sacral canal for a distance of 1 to 1½ inches. Once the needle is inside, it is wise to aspirate it with a syringe to be sure that a blood vessel has not been tapped. After this, we usually inject a small amount of saline, which should go easily (sometime the needle bevel is lying between the bone and periostium thus making the injection difficult). In either case, the needle has to be withdrawn for a short distance, reinserted at a different angle, and its position checked once more.

After correctly placing the needle in the peridural space, injection begins. However, we think it wise to double-check the technique, to make sure the needle has not entered the subarachnoid space. For this purpose, we use the Stookey-Quenkesteat method, for raising the spinal fluid pressure; if the subarachnoid space has been punctured, the spinal fluid will flow from the needle due to the increased pressure. (Sometimes the subarachnoid space can be punctured, but because the spinal fluid pressure is low, no fluid will be obtained, even though aspiration is resorted to.) This technique consists of three maneuvers: 1) bilateral compression of the superficial jugular; 2) bilateral compression of the deep jugular; 3) compression of the abdomen with the fist, the patient having the abdominal muscles relaxed.

After these maneuvers are applied, we have the patient cough hard, thus raising the spinal fluid pressure. If no fluid is obtained by any of these procedures, we consider the needle to be outside the subarachnoid space and begin the injection.

The entire amount of anesthetic can be given in one single dose, However, the single injection technique is not the best for many reasons, such as:

1) When a large amount of fluid is injected peridurally in a short time, the intravertebral pressure is suddenly raised; since the external boundary of the peridural space cannot be distended (bone), the meningeal dura and arachnoid are compressed and the spinal fluid squeezed upwards; therefore, the intracranial pressure increases and often causes epileptoid phenomena, which are very disagreeable.

2) If the needle is in the subarachnoid space without the anesthetists' knowledge (which seldom occurs if all the aforementioned precautions have been followed), a massive injection in the subarachnoid space is given, with all its consequences (massive spinal anesthesia and spinal bulb block, followed by circulatory and respiratory collapse).

For these reasons we like to divide the total dose in three portions given at intervals. The first one, which should be a dose equivalent to the one used for spinal anesthesia (5 cc procaine 2 per cent or 5 cc pontocaine 0.2 per cent) is given immediately after the puncture is performed. After 5 to 7 minutes elapse, the patient's legs and buttocks are checked by pin prick for anesthesia; we also check the voluntary movement of the toes, but find this not very dependable, since in some cases of spinal, the patients are capable of this action in the beginning of the anesthesia. In case there is anesthesia, meaning that a subarachnoid tap was mistakenly done, the needle is withdrawn and the operation carried on under spinal. If no anesthesia is denoted, the second dose is given—10 cc, and a new interval of 3 to 4 minutes is taken, so that the solution will have time to spread. After this, or 10 to 11 minutes after the first dose, a new check of the legs and buttocks for anesthesia is done. In case it is negative, we are sure that the subarachnoid space has not been entered, and inject the remainder of the solution, i.e., 18 to 25 cc.

The total amount of solution used varies slightly according to the patient's weight; we use between 33 and 40 cc of 2 per cent procaine or 0.2 per cent pontocaine. In the higher punctures, a smaller amount should be given, never exceeding 25 cc of the same solutions in the cervical or high dorsal peridural space. Also, smaller amounts are given in the sacral peridural space, the average being about 25 to 30 cc of 2 per cent procaine or 0.2 per cent pontocaine.

SUMMARY AND CONCLUSIONS

A description of peridural anesthesia and its use in urological surgery are presented. The technique of the lessened resistance (Dogliotti), which has been routinely employed with very satisfactory results for the past 15 years on the urological practice of Dr. J. Silva de Assis and the author, has been slightly changed in order to save time. However, the results are the same. Tables 1 and 2 present a summary of 134 major operations and the anesthesias used. The results of peridural injections of diodrast and neo-iopax, done in order to learn the final distribution of the solutions, are presented also.

An association of peridural with sodium pentothal dissolved in the intravenous fluid administered during the operation is described; this being very helpful in cases of uncooperative patients and in cases where touch sensation persists after the anesthesia is completed. It was used in 15 cases or 11.2 per cent of the peridurals done.

Among over 1,000 peridural injections, two fatalities were encountered. Measures of safety and prevention of accidents have been described together with different techniques for peridural puncture; of these, the technique of the lessened resistance is considered to be the best one.

Peridural is the anesthesia of choice: 1) in poor risk patients (with bad circulatory system; bad respiratory system; high blood pressure; low blood pressure); 2) in long operations, because of its longer duration and minor anesthetic shock; 3) in operations above the umbilical level, where a spinal anesthesia would bring an increased danger.

We only resort to spinal anesthesia in patients whose conditions are safe for it and where the operative procedure is of short duration and permits a low spinal. Spinal anesthesia is also the choice for transurethral manipulations. General anesthesia is left for those patients who are unco-operative, such as children and a few adults.

We agree with those who say that peridural is technically much more difficult than spinal anesthesia; it also takes more time to perform. But, if the safety of the procedure, the longer duration of the anesthesia, the absence of postanesthetic headaches, etc., are counted, a lot of credit will be given to peridural —and, as far as pain prevention and muscular relaxation are concerned, the results of spinal and peridural anesthesia are the same.

Rua São Paulo, 1801, Belo Horizonte, Brazil.

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THE PISTOL GRIP MODIFICATION OF THE STERN-McCARTHY RESECTOSCOPE

THOMAS E. GIBSON

From the Department of Urology, St. Josephs Hospital, San Francisco, Calif.

The basic design of the Stern-McCarthy resectoscope has changed very little since its inception. It is still the instrument of choice with most urologists. The fact that it has stood the test of time without any revolutionary change in design is a tribute to the men concerned with its development. Mr. Fred Wallace, President of American Cystoscope Makers Incorporated, has listened sympathetically to a vast number of proposals for modification of the instrument and has patiently carried out the whims of many resectionists, including my own.

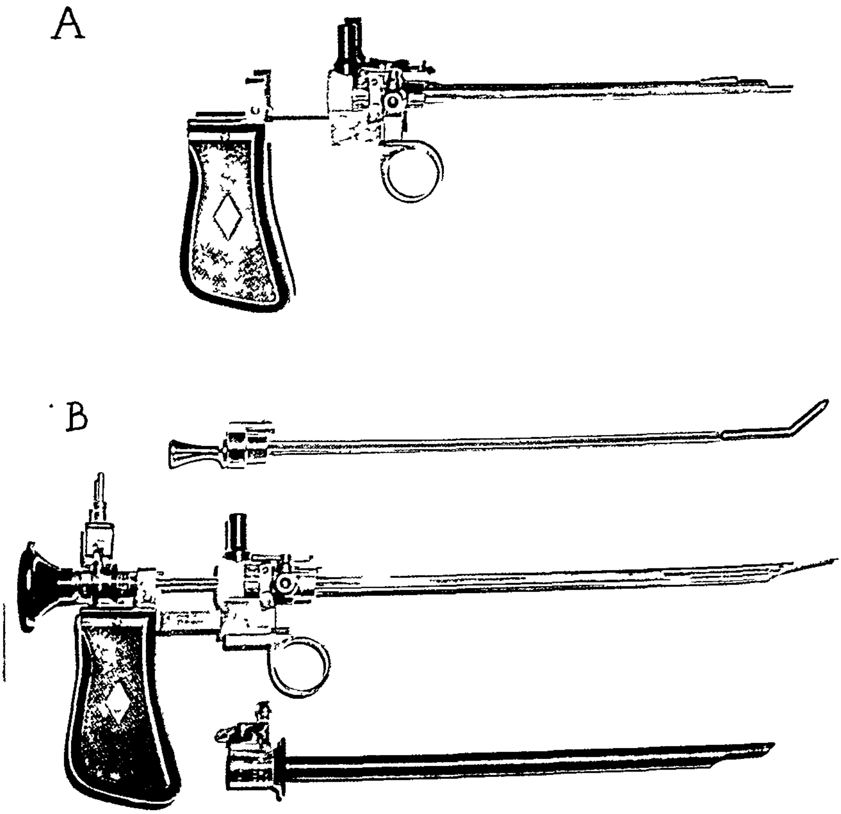

FIG. 1 Photographs of modified Stern-McCarthy resectoscope *A*, working element alone, *B*, complete assembly.

Probably the most important modification was that of Nesbit[1] permitting third dimensional perception during resection. His instrument could be operated

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[1] NESBIT, R. M J Urol , 47: 200-201, 1942

readily with one hand leaving the other hand free so that a finger could be inserted in the rectum, thus enabling the operator to more accurately gauge the amount of tissue which should be removed, and also to push depressed tissue upward into the path of the loop.

It was believed that the same result could be achieved with a pistol grip instrument which would facilitate the operation of the instrument, at least in my hands, since it could be operated with the trigger finger rather than the thumb. Accordingly, a standard Stern-McCarthy working element was made over with the aid of a local instrument maker who carried my ideas[2] to a very satisfactory conclusion. This local makeshift instrument has now been in use for 10 years and proved so satisfactory in operation that Mr. Wallace was prevailed upon to manufacture it. His version of the instrument is shown in figure 1. The carriage slides to and fro on a double bar with a spring mechanism which automatically carries the loop back to its original cutting position. The action is similar to that of the Baumrucker resectoscope in that the motivating power for pulling the loop through prostatic tissue is supplied by the forefinger rather than the thumb, a complete reversal of the Nesbit mechanism. The instrument accommodates the McCarthy foroblique telescope, and uses standard McCarthy electrotome sheaths and loops.

In personal experience, the pistol grip modification has greatly facilitated rapid and accurate cutting.

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Gibson, T. E.: J. Urol., 47: 200-201, 1942.

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A NEW TYPE OF ARTIFICIAL KIDNEY. I. TECHNIQUE

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The use of an artificial kidney in specific clinical conditions associated with both acute and chronic uremic states has led to many modifications of the basic instrument of Kolff.[1] Its use in experienced hands presents little danger to the patient. The type of kidney described in this report is a simpler, more compact unit than the one previously reported[2] and has as well other advantages.

The basic principle of all artificial kidneys based on dialysis is essentially the same. Blood flows from an artery, through a cellophane tube or exposed to a cellophane membrane and returns to a vein. A practical appliance should fulfill the following ideals: 1) easily and readily portable, 2) simple design and construction, 3) easy to assemble and repair, 4) capable of sterilization, 5) a large area of dializing surface related to a small volume of blood in the apparatus, and 6) ability to maintain a low metabolite concentration in the diffusing fluid.

Bearing in mind these requirements, we have further improved our artificial kidney to consist of an apparatus measuring 9 by 11 by 5 inches which weighs approximately 10 pounds fully assembled. The basic filtration unit consists of a sheet of "plain tissue" cellophane between a pair of plates forming a thin chamber. Through this unit the blood passes on one side of the cellophane sheet and the perfusing fluid on the other. Such multiple chambers, held together under pressure, comprise the artificial kidney (fig. 1).

Each plate (fig. 2) is a solid sheet of bakelite measuring 7 by 9 inches by 0.043 inches thick. There are nineteen feeder channels (fig. 3), each measuring $\frac{1}{8}$ inches wide and $7\frac{1}{8}$ inches long, which are cut along the long axis of the plate. These are 0.025 inches deep. The channels are connected above and below at each end. Two feeder channels are cut between the conduits at the two corners on only one side of the plate. Depending upon the position of the feeder channels, either blood or perfusing fluid only will flow through each chamber. The plates are so superimposed that the feeder channels carry blood and perfusing fluid separately to and from each plate to the opposite sides of each cellophane membrane.

Two bakelite plates are used for the internal surfaces and two aluminum plates for the exterior surface as covers. These measure 9 by 11 inches. Holes are bored along the outer inch of the aluminum plates to permit screws and bolts to be passed in order to hold the assembled kidney together under pressure. Only the two top covers have four additional openings, two for perfusing fluid and two for blood. To fit these openings, special bakelite nozzles with a precision centerhole bored into them permit the fitting of any standard needle adaptor hub.

The apparatus is aligned in order as follows: 1) top aluminum cover plate, 2) top front bakelite cover plate, 3) bakelite grooved plate, 4) cellophane sheet, 5)

Accepted for publication May 20, 1952.

[1] Kolff, W. J : New Ways of Treating Uremia. London: J & A Churchill, Ltd., 1947.

[2] Sterling, J. A. and Doane, J. C.: New type of artificial kidney. Urol. & Cut. Rev., 53: 385, 1949.

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bakelite grooved plate with the pair of feeder channels on the opposite side aligned to the feeder channels of the following plate, 6) bakelite grooved plate with feeder channels coinciding to the preceding plate, 7) cellophane sheet, 8) grooved bakelite plate with feeder channels opposite and so forth to the 9) bottom bakelite cover plate, and 10) bottom aluminum plate (fig. 4).

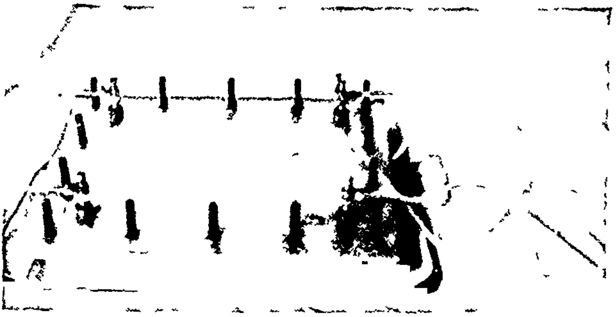

FIG. 1. Photograph of artificial kidney. Aluminum top plate and bolts can be seen Three way stopcocks and tubing are attached.

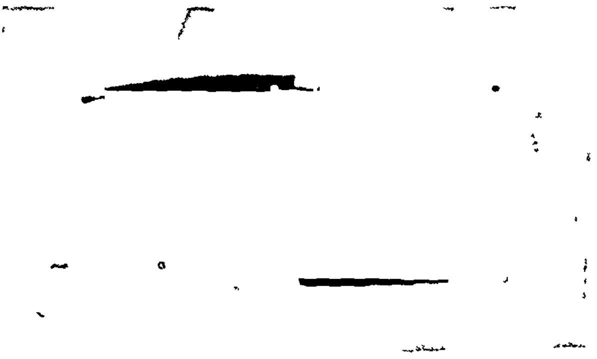

FIG 2. Photograph of both front and back views of bakelite plates. Front view shows 19 feeder channels. Rear view shows two feeder channels cut between corner conduits on one side of plate.

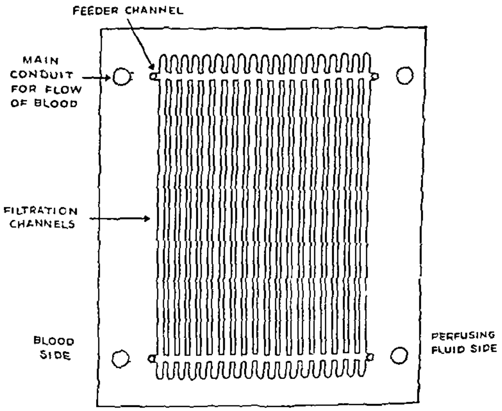

FIG 3 Diagram of bakelite plate

Blood enters the filter through the right upper conduit and is fed into the even-numbered blood chambers, since the feeding channels on the even (or right side) are directed towards the source of the blood. After passing through the chamber, the blood leaves through the lower feeding channels, on the same side (right) as the entrance of the blood. A similar route is followed by the perfusing fluid on the opposite (left) side of the apparatus, since in these the feeding channels are so arranged to be all on the left.

Effective surface dialyzing area of each plate was computed to be 18.1 sq. inches or 116.8 sq. centimeters. Each chamber contains 0.4601 cu. inches or 7.55 cu. centimeters of fluid or blood. Hence in a 20-blood chamber apparatus, 150 cu. centimeters of blood would be present. The chambers are effectively sealed from leakage or contamination by the pressure exerted between the cover plates as they are tightly bolted together. The nozzle attachments are bakelite. These are constructed to screw tightly into the cover plates, so that no leakage is present. The centers are so bored as to permit any standard 3-way stopcock or needle adaptor hub to fit. Abbott pyrogen-free plastic tubing is attached to the 3-way stopcocks directly to both blood and fluid inflow and outflow tracts.

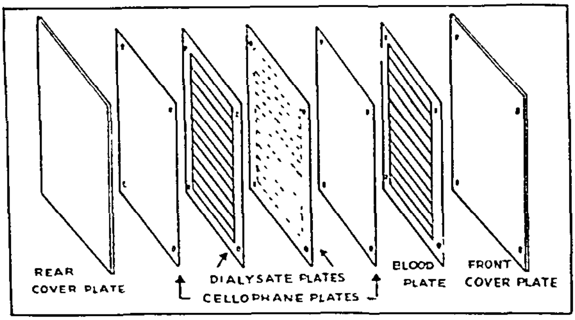

FIG. 4. Diagram of artificial kidney: Exploded view. *1*, Front aluminum plate. *2*, Front bakelite plate. *3*, Bakelite grooved plate. *4*, Blood chamber. *5*, Cellophane filter sheet. *6*, Perfusing fluid chamber. *7*, Bakelite grooved plate. *8*, Perfusing fluid chamber. *9*, Cellophane filter sheet. *10*, Blood chamber, etc. to rear cover plate.

The pump consists of two units. The first unit, which is in actual contact with blood is constructed of bakelite. It is a piston type positive displacement pump with stainless steel piston cylinders and ball check valves. It is constructed so that any standard needle adaptor hub, which is attached to tubing, can fit into it without leakage. This piston pump is used to return the patient's blood from the kidney to an elevated container. Blood turbulence is eliminated. With its use, blood in the apparatus is under varying pressure. It is capable of operating at very low flows (10 cu. centimeters per minute). The pumping rate of this unit can be changed by adjusting the effective crank length by means of a small screw which also serves as the crankpin (figs. 5 and 6).

The second unit is used to circulate the dializing fluid and its pumping rate is not adjustable. It consists of a positive displacement pump which moves the fluid through a plastic or rubber tube placed in the pump, by means of two ball bearing bakelite grooved plate with the pair of feeder channels on the opposite side aligned to the feeder channels of the following plate, 6) bakelite grooved plate with feeder

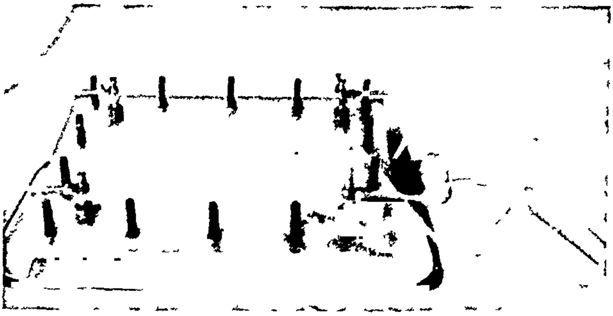

Fig 1. Photograph of artificial kidney. Aluminum top plate and bolts can be seen. Three way stopcocks and tubing are attached.

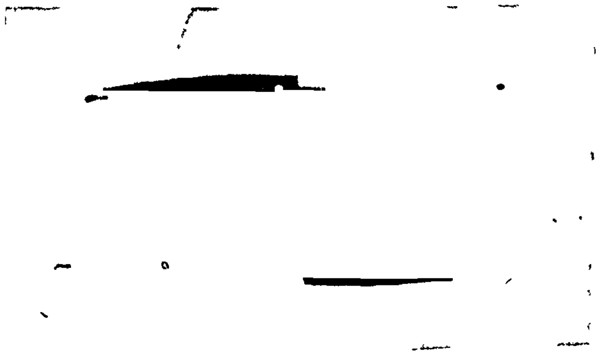

Fig. 2. Photograph of both front and back views of bakelite plates Front view shows 19 feeder channels. Rear view shows two feeder channels cut between corner conduits on one side of plate

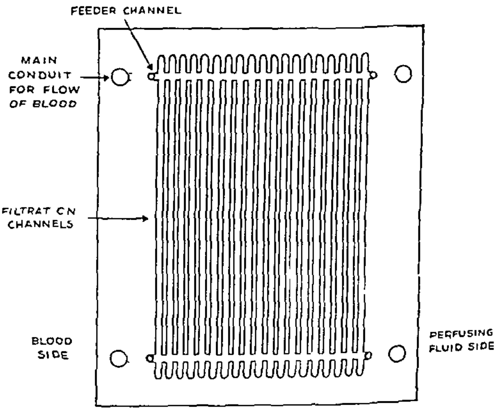

Fig 3 Diagram of bakelite plate

channels coinciding to the preceding plate, 7) cellophane sheet, 8) grooved bakelite plate with feeder channels opposite and so forth to the 9) bottom bakelite cover plate, and 10) bottom aluminum plate (fig. 4).

Our routine perfusing fluid has been 5 per cent glucose in half-normal saline. At times hypertonic glucose, or plasma, is used in an effort to withdraw fluid from the patient or to prevent or treat pulmonary edema. Our clinical experience has shown that the various formulas suggested[3, 4] for perfusing fluid have been unnecessary to accomplish the purpose of removing metabolites. To correct metabolic disturbances which may arise during the procedure, solutions of calcium or base may be given parenterally to the patient. Only rarely, as in sudden potassium ion disturbances, is potassium added to the perfusing fluid. Elevation of perfusing fluid temperature over room temperature, while it may slightly promote increased ion exchange between blood and bath, has been abandoned as a routine procedure. The elevated temperature, in our opinion, tends to 1) increase hemolysis and clotting, 2) promote febrile reactions and 3) lead to an increase in the blood pressure of the patient.

To overcome the serious obstacle of clotting during the procedure, all parts in actual contact with blood have been selected to minimize clotting formation. These consist of bakelite plates and attachments, plastic tubing and a plastic blood filter. Only at the connecting points of the tubing (which consist of stainless steel or aluminum adaptors), two small stainless steel ball bearings in the pump and in the glass air trap is the procedure vulnerable to clotting. This may be further minimized, if desired, by coating the air trap with silicone.

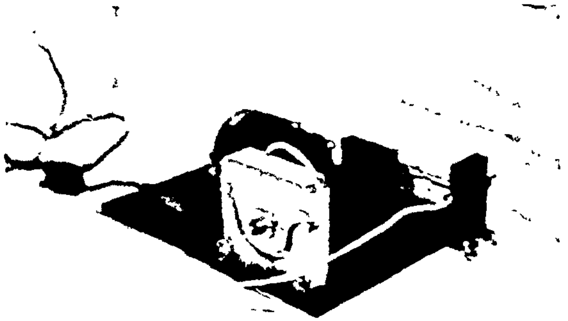

FIG. 7. Photograph of pump. Both piston type, for blood, and positive displacement pump, for perfusing fluid as shown.

The procedure of rinsing the kidney apparatus both before and after autoclaving with sterile distilled water tends to diminish pyrogen reactions which may be attributed to the small quantities of glycerine coating which remains from the manufacture of the cellophane sheets.

PREPARATION OF THE APPARATUS

The kidney pack. Each of the bakelite plates are thoroughly scrubbed with detergent and water, then washed several times with pyrogen free distilled water. The plates are replaced in the apparatus together with the cellophane sheets and

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[3] Wener, J. and de Leeuw, N. K. M.: Role of potassium in dialysing fluid in treatment with the artificial kidney. Proc. Soc. Exp. Biol. & Med., 71: 18, 1949.

[4] Kolff, W. J.: Artificial kidney. Clev. Clin. Quart., 17: 216, 1950.

rollers mounted on a rotating disk. These rollers squeeze the tube closed and move the fluid through the tube in this manner. The outstanding feature of this unit is the fact that the fluid, which is corrosive to metals, does not come in contact with any metal part. The tubing can be removed or placed in the pump by means of a small side plate fastened with wing nuts.

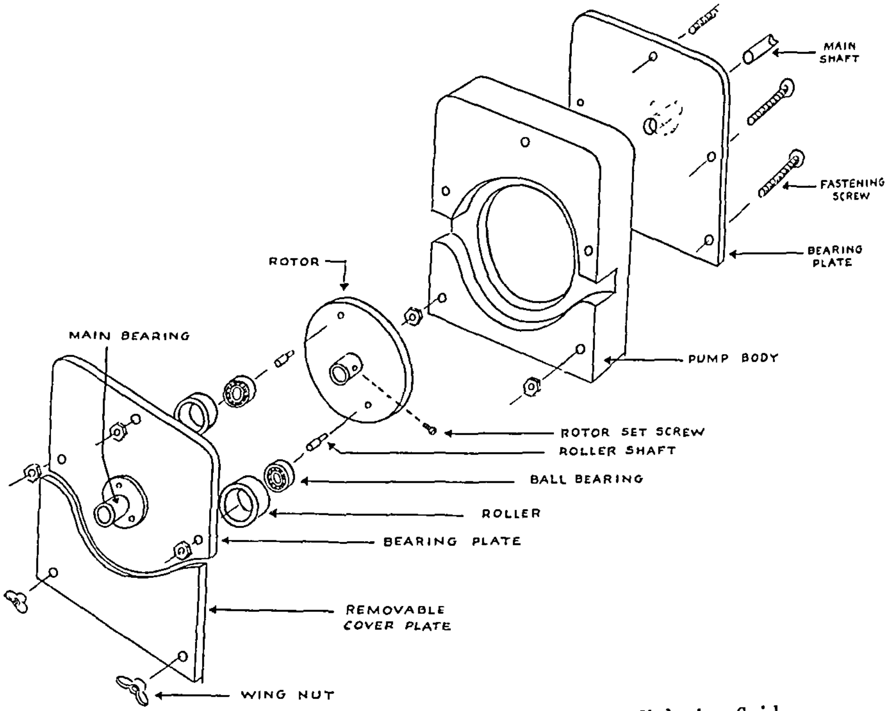

FIG. 5. Exploded view of circulating pump for dialyzing fluid

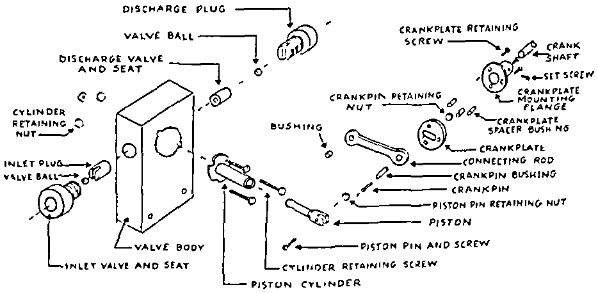

FIG. 6. Exploded view of blood pump

Both units are operated from the same shaft which is rotated through a two to one gear reduction by a small 110 volt A.C. motor with a geared head (fig. 7). The speed of the shaft is approximately 100 r.p.m. The entire section, through which the flood flows, can safely be autoclaved and easily mounted to the remainder of the pump.

corrected prior to dialysis. Edema or other evidence of over-hydration should be corrected, even though it is possible to remove water in addition to retained metabolites with dialysis.

A careful preliminary period of observation and preparation of the patient previous to dialysis is essential in order to decrease the risk and complications of the procedure. A complete history and physical examination should be done. Renal function studies should include blood urea nitrogen, nonprotein nitrogen, complete urine analysis, urine volume and intake of fluids. The coagulation time (Lee-White method of determination is used), prothrombin time, complete blood count, hematocrit, and blood specific gravity should be known. These are determined just prior to starting the procedure. Blood chemistry studies consist of total serum proteins (including A/G ratio), chlorides, carbon dioxide combining power, total base and serum potassium. A complete cardiovascular investigation, including electrocardiogram, venous pressure and circulation time, as well as clinical evidence of heart failure is determined.

All necessary clinical and laboratory studies are to be completed at the time dialysis is to be started. Daily injections of 600,000 units of penicillin are to be started on the day previous to the procedure. Shortly before starting, a quick-acting barbiturate may be given to the patient, if needed. Morphine or Demerol may be used cautiously. The general condition and color of the patient are carefully noted and followed. During the actual procedure the patient is checked every 15 minutes with blood pressure, pulse, respiratory rate, temperature and color noted; to be followed by half hour readings for 6 hours at the end of the procedure. Blood for complete studies is drawn from the arterial cannula at both the beginning and end of the procedure.

Both the arm and leg of the patient on the selected side are prepared and draped. Under local anesthesia the radial artery and the saphenous vein are cannulated, inserting and tying in the plastic cannulae. When both cannulae are in place, heparin is administered into the venous cannula using for the first dose approximately 1 mg. of heparin per kilogram of body weight. Additional heparin is given as needed to keep the coagulation time about 30 minutes. To prevent oozing from the incision while the patient is heparinized, a pressure bandage is placed around the incision and if needed, an ice pack is added. To stop further oozing thrombin can be applied to the wound.

ASSEMBLING THE APPARATUS

The artificial kidney is placed on a table close to the patient. The plastic tubing previously described is used throughout. While the surgeon is preparing the patient, the kidney is rinsed with sterile pyrogen free distilled water. As the diagram (fig. 8) shows, the tubing is placed as follows: Two bottles of bath solution are attached to the 3-way stop-cock at the inflow end of the bath nozzle. To the inflow nozzle of the blood section a blottle of plasma is attached to one opening of the stop-cock; the other opening being used to connect the arterial cannula to the kidney. The remainder of the plastic tubing is attached to both outflow nozzles, the pump, air trap and to the venous cannula of the patient. The air trap merely the entire kidney is bolted together. After the four nozzles are screwed in, both sides of the apparatus are flushed with three liters of pyrogen distilled water. The "kidney pack" contains the assembled kidney, six 3-way stopcocks (including two extra) and the pump assembly. These are wrapped together and autoclaved.

Additional accessories to be used with the apparatus are assembled as follows:

1) Tubing is to include three Venopak (Abbott) disposable tubing for connecting patient to kidney and bath bottles to kidney; three Donopak-48 (Abbott) tubes for connecting kidney to pump and pump to air trap; two RC-Pak (Abbott) with plastic filter drip to connect the air trap to patient's vein and the plasma to the kidney; and eight 10 cc and six 2 cc syringes.

2) A sterile venesection pack including instruments for artery and vein cut down is provided. This is supplemented by a) two additional plastic cannulae, b) three 3-way stopcocks, c) novocaine 1 per cent, 60 cc, d) iodine and alcohol for skin preparation, e) sterile towels and gauze, f) drainage pads and 3 inch gauze bandage, g) fibrin. All items except d, f and g are to be autoclaved individually and for use in the insertion of radial artery and internal saphenous cannulae.

3) Further accessory equipment is to include a) standards and supports for flasks containing bath solutions, b) solutions for use as bath, all pyrogen free, to include 10,000 cc of 5 per cent glucose in normal saline, 2000 cc of 5 per cent glucose in distilled water, c) empty liter flasks for use in collecting bath returned from kidney, d) special suction pump for accelerating return of blood from kidney to patient, e) lamps, heaters, hot water bottles and electric pad, f) two liters of cross-matched blood, g) two bottles of plasma and h) 1000 mg. heparin.

4) Emergency equipment for correction of electrolyte and volume changes and for administration in event of catastrophe must be at hand. These include solutions for adjustment of fluid and electrolyte balance: a) sodium lactate, 2 liters; b) ammonium chloride, 2 liters; c) sucrose and glucose, 100 cc of each in 50 per cent concentration; d) 5 per cent glucose in ½ normal saline, 10 liters; e) protamin sulfate; f) phlebotomy set and citrate containing empty flasks, two. In addition, adequate blood, at least 1500 cc, and plasma, three units, are to be available. Oxygen, to be used either by catheter or through positive pressure mask, is provided. An emergency drug kit is provided to include syringes, alcohol lamp, hypodermic, intravenous and intracardiac sterile needles; drugs consisting of atropine, adrenaline, caffeine, coramine and metrazol.

5) The necessary laboratory equipment needed at the bed side is to include 12 oxalated tubes, 30 clean test tubes, hematocrit tubes, blood cell pipettes, coagulation tubes, copper sulfate solutions (for specific gravity estimations) and a direct writing electrocardiograph.

PREPARATION OF THE PATIENT FOR DIALYSIS

Many factors are to be considered in the selection of the proper patient to undergo dialysis. Generally the patient should have a blood urea nitrogen greater than 100 mg. per cent. Details as to previous or present renal or cardiovascular disease must be known and controlled as much as possible. A fairly adequate liver function should be present. Anemia and hypoproteinemia must be

POST-DIALYSIS PRECEDURE

Following the dialysis the cannulae are left in the veins and sterile stylets replaced, with a compression bandage placed over the wound. Regardless of the appearance of the patient, he is treated as is a shock patient, with temperature, pulse, respiratory rate and blood pressure readings every thirty minutes for the next 6 hours. A coagulation time is taken two, four and twelve hours later, and thereafter as indicated. Penicillin is continued for the next three days. At the end of six hours blood is taken for a blood urea nitrogen. Both twelve and twenty-four hours later, and there-after as indicated, complete blood and urine studies are repeated.

Prior to disassembling the apparatus, the artificial kidney is drained of blood and bath fluids. Both sides are rinsed with distilled water until the outflow fluid is clear; as is also the pump mechanism. Bolts are removed and the bakelite plates are scrubbed and left to soak in distilled water. All tubing, cellophane sheets and air trap are discarded.

SUMMARY

A portable apparatus for extrarenal hematodialysis has been developed. The use of bakelite plates and cellophane sheets in the construction of the kidney, a pump constructed of bakelite and the use of plastic tubing decrease the tendency of blood to clot. A new type of pump both to circulate the blood and also the perfusing fluid is described. Complete technique in its use is presented.

The artificial kidney in experienced hands is a safe and efficient method for temporarily replacing the excretory function of the kidney.

The authors wish to acknowledge the scientific and engineering contributions to the construction of the artificial kidney by Mr. William Bernard, B. A.

consists of an empty 1 liter bottle fitted with a needle adaptor and the RC-Pak (Abbott). Plasma is started through the artificial kidney both to check it for leakage prior to attaching the patient and also to fill in the "dead space" of the kidney and tubing. Leakage through the cellophane plates is manifested both by color change and foaming in the bath liquid. A clear bath solution after running through the plasma indicates that all the cellophane plates are intact.

THE PROCEDURE

During the actual operation of the artificial kidney, every 30 minutes blood is taken for laboratory determinations. Done immediately, whenever practical, are blood urea nitrogen, carbon dioxide combining power, blood specific gravity, hematocrit and coagulation time. Any of these determinations may be repeated oftener depending on whatever the situation arises. Additional therapy or changes in the perfusing fluid are done according to either the laboratory results or the clinical condition of the patient. Effort is made to keep the coagulation time at a constant level of thirty minutes and both specific gravity and carbon dioxide combining power at normal levels. Electrocardiographic tracings are taken frequently to grossly gauge the potassium ion status of the patient.

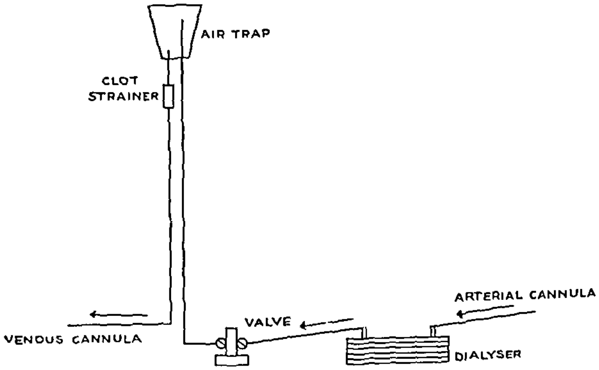

FIG. 8. Diagram illustrating operation of artificial kidney. Blood enters apparatus either by force of arterial blood pressure or by pump, or both. Pump raises blood to air trap, where force of gravity returns it to vein.

Additional observations are made on the perfusing fluid. Every thirty minutes samples are taken. Immediate observations are carried out for red blood cells (benzidine test). Volumes of all types of fluid used in the dialysis are recorded and on all samples, determination of blood urea nitrogen, nonprotein nitrogen, creatinine, calcium, potassium and protein content are made.

Both control of flow and of the bath solutions is aided with the use of 3 way stop-cocks, height control and the use of the pump. The blood flow through the kidney is controlled by use of either the pump and clamps on the tubing, as well as adjusting either the height or the amount of air in the air trap.

At the close of the procedure notes of both the type and flow of bath fluids are recorded. Total outflow of perfusate is known. The amount of blood remaining in the air trap, as well as additional blood which may have been given, is noted. Necessary clinical facts pertinent to the patient are added to the other data

1950 his red blood cell count had reached 3.51 million, with a hemoglobin of 10.2.

Because of the persistent hematuria with resulting anemia and a perfectly normal right kidney, it was decided to do a left nephrectomy. This was performed in the usual manner, with a left subcostal incision. The kidney was easily separated from the surrounding structures and grossly appeared normal. It was sent to the pathologic laboratory intact and sectioned serially. The pathologic report is as follows:

"S-51-741, hospital No. 131165. Diagnosis: Consistent with hereditary hemorrhagic telangiectasis of kidney; early intrapapillary nephrolithiasis. The gross specimen consists of a left kidney submitted in the fresh state and weighing 117 gm. The external surface of the structure is reddish brown in color, smooth and glistening. The capsule is stripped with ease. The specimen retains a suggestion of fetal lobular pattern. There is a moderate amount of pale yellow fat in the pelvis which is somewhat hemorrhagic in appearance. The short stump of the ureter is lined with a smooth, glistening gray-white mucosa. On cut section through the specimen, the cortex and medullary portions of the organ are well demarcated, one from the other. The cortex measures 8 mm. in thickness and is glistening and reddish brown in color and appears homogeneous throughout. The renal pyramids are a lighter reddish brown in color and show prominent linear striations of alternate gray-white and darker purple red streaks. The arcuate vessels are prominent but do not stand widely patent, but are soft and collapsible. The renal calyces are not dilated. No stones are present. The mucosa is gray-white in color with a few scattered areas of purple red hemorrhagic mottling. On opening into the calyces, the renal papillae examined show a slight granular irregular purple red 'spider web' like discoloration. Also noted in one renal pyramid there is a small 1 mm. rounded, purplish-blue cystic-like area. There are no other lesions noted in the kidney on gross examination. Total, seven blocks.

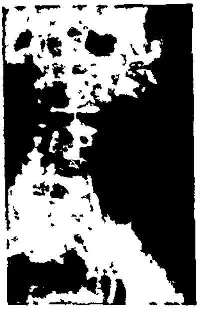

FIG. 1

"Microscopic (figs. 2 and 3): Slide 1 was taken from the area indicated. The glomeruli do not appear unusual. The tubular structures are well preserved and no alterations in their cellular detail are encountered. In the area cribosa, near the apex of the papilla, many of the papillary ducts (of Bellini) are cystically dilated and contain a pale, eosinophilic, hyaline material. Aside from this alteration, this section of the organ does not appear unusual.

"Slide 2, representing 1 block but 4 sections, presents essentially the same

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HEMORRHAGIC TELANGIECTASIS: CASE REPORT

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This clinical entity was recently covered by Campbell, who adequately describes the histology, pathology, diagnosis and treatment. He stated that up until 1949, less than 30 cases had been reported. This is to add another proven case to the literature.

A 46-year-old colored janitor was admitted to Grady Memorial Hospital on November 11, 1950 because of blood in his urine. He enjoyed good health until July 1950, when he noted the onset of a painless gross hematuria, accompanied by slight frequency and nocturia, three to four times. Since its start, the hematuria was constant, although he noticed that his urine was more clear when he drank large quantities of water. He passed an occasional clot, but was never in retention, had no hesitancy or diminution in the size and force of his stream. Three weeks prior to admission, the patient consulted a urologist who gave him four injections of penicillin and some oral medication to "build him up." He was having some weakness and a tired feeling, some shortness of breath on exertion, and lost 12 pounds in the last 5 months.

The patient's history disclosed that in 1930 he had had a similar episode of painless hematuria which lasted three months. He was treated by an "herb doctor."

Physical examination was essentially negative. Blood pressure was 120/70; neither kidney was palpable and no masses or tenderness were found. The prostate was of normal size, shape and position.

On November 11, by cystoscopic examination, gross blood coming from the left ureteral orifice was the only positive finding. The pyelograms and ureterograms were normal, except that in the infundibulum of the left superior calyx, there was a slight deformity consisting of a shallow filling defect about 2 to 3 mm. in length (fig. 1).

Extensive laboratory work was done on this patient, with the following results: Urine: pH 6.0; specific gravity 1.017; 2 plus albumin; sugar negative; innumerable red blood cells; occasional white blood cell; no casts; no bacteria. Urine cultures were persistently negative. The total output of phenolsulfonphthalein in 1½ hours was 75 per cent. Red blood cells, 2.5 million; hemoglobin, 9; white blood cells, 3,500; eosinophiles, 2; 68 segs., 26 lymphs, 4 monocytes. Kahn negative. Bleeding time was 2½ minutes, clotting time 6 minutes. Prothrombin time was 14 seconds, control undiluted 15 seconds. Nonprotein nitrogen 39 mg. per cent. Platelet count 314,600. Tuberculin test was negative in the first strength and mildly positive in the second. X-ray of the chest was negative.

On two more occasions blood was seen coming from the left ureter, and pyelograms demonstrated the filling defect in the left major infundibulum. The patient continued to bleed, necessitating several blood transfusions. By December 14,

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"Slide 3, representing 1 block but 5 sections, presents essentially the same findings as described above. The thin-walled, tortuous vessels, however, appear more prominent, and in one area, the pelvic mucosa is absent immediately over the dilated blood vessels. There is, however, no evidence of extravasation of red blood cells through the vessel walls, nor into the surrounding supporting tissues.

"Slides 4 and 5 are believed to have some from the same pyramids (see fig. 3). They present no unusual or abnormal features.

"Slide 6, (five sections) presents essentially the same findings as seen in sections 2 and 3.

"Slide 7 (five sections) presents at the apex of one of the papillae a tiny bluish, calcified area between several of the dilated papillary ducts. The surrounding tubules are somewhat more dilated than in the preceding sections, but aside from these alterations, the changes are the same as previously described."

SUMMARY

This is to report a case of hemorrhagic telangiectasis as diagnosed postoperatively by means of pathologic sections.

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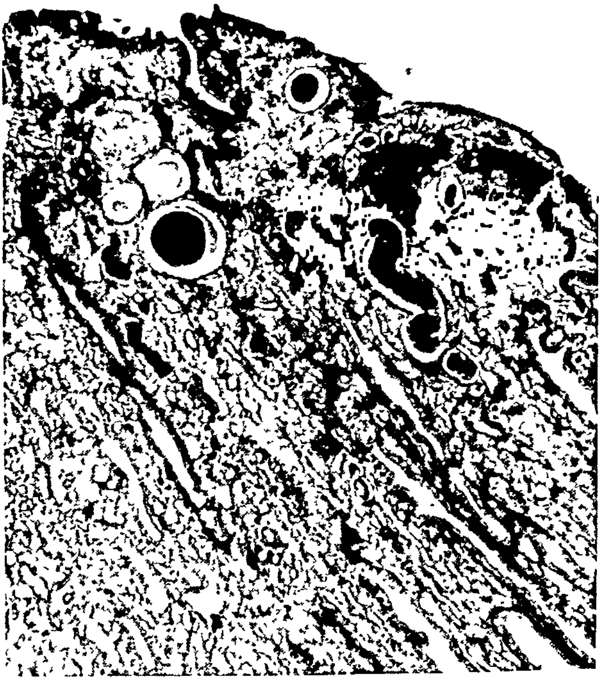

FIG. 2

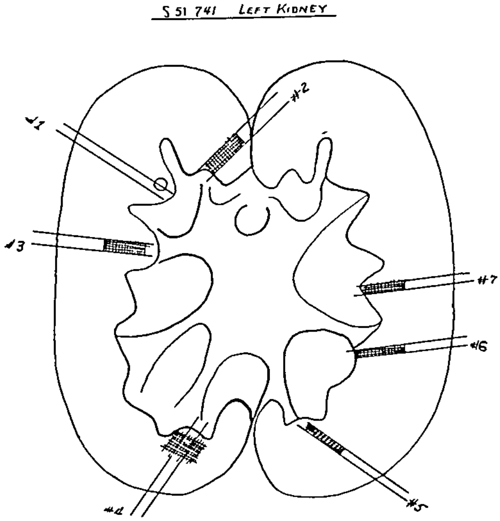

FIG. 3. Left kidney. Scarred areas indicate sites at which minute deviations from normal were observed at gross examination.

findings as slide 1, but in addition, immediately under the pelvic mucosa, among the dilated, cast-filled papillary ducts, are a few extremely thin-walled, tortuous, blood-filled vessels, situated among the dilated ducts. The remaining kidney parenchyma does not appear unusual.

Waring and Drane[2] (1932) reported a case of a seed-bearing grass which had been put into the urethra and disappeared. The man developed symptoms of renal suppuration. A nephrectomy was done and the grass was found in the renal pelvis. Brattstrom[3] (1927) also reports a straw having been lost in the urethra and ascending into the kidney pelvis from where it was removed surgically. Kretschmer[4] in 1916 demonstrated that reverse peristaltic action does at times occur on stimulation even in a normal bladder and ureter. Senger[5] (1933) found two pieces of toothpick that had ascended from the bladder into the kidney pelvis.

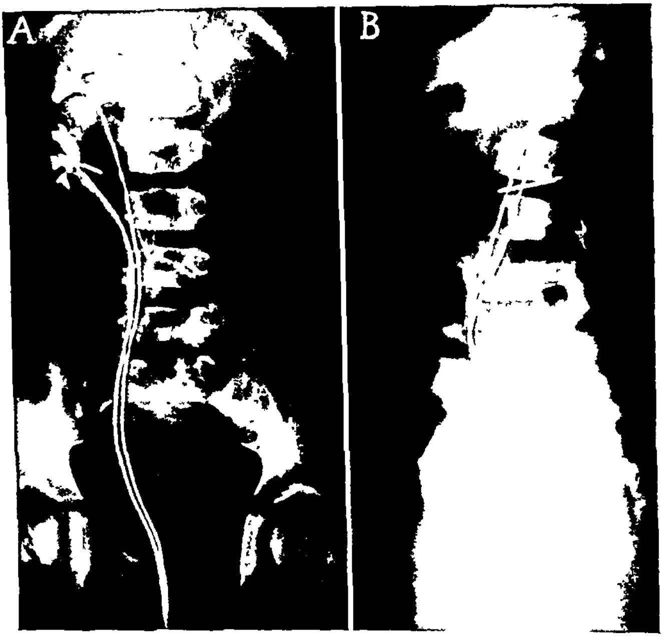

FIG. 1. *A*, anteroposterior pyelogram showng pin in region of lower right pelvis. *B*, lateral pyelogram coroberating findings in *A*.

There are also in the literature several instances of indisputable documentary evidence of extraneous objects having passed from the duodenum into the right kidney. Capon and Wells[6] (1938) found a Kirby hair slide with one end in the duodenum and the other in the right kidney. Mackay[7] (1947) also found a bobby pin that had perforated the second portion of the duodenum and had entered the right kidney pelvis.

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A BOBBY PIN IN THE KIDNEY PELVIS

O. A. NELSON, A. W. KRETZ, J. L. McCORMACK, J. M. DOCTER AND C. W. DOUGLASS

The unexplained presence of a bobby pin in the kidney pelvis of a 4-year old girl seems worth reporting. According to the parents, she had always had enlarged tonsils. Six weeks before the urological examination she had a skin rash, sore throat and fever. The diagnosis was scarlet fever. Soon after the fever subsided, gross hematuria occurred on several occasions. Two weeks before entering the hospital for a urological study a tonsillectomy was performed. This was followed by moderately severe bleeding from the tonsillar bed.

On the evening before the urological examination, the child was seized by severe pain in the region of the right kidney. A few minutes later she passed clots of blood from the bladder; then, the pain ceased.

On April 4, 1950, she was admitted to the Swedish Hospital. General examination revealed the pulse, temperature and respiration to be normal. Tenderness and muscular rigidity were present over the right kidney. The hemoglobin and blood count were normal. The urine contained much blood but was otherwise normal to laboratory examination.

A roentgenogram of the abdomen revealed a dense shadow in the upper quadrant. A film exposed in the lateral position showed the opaque object to be too far posteriorly to be in the gastro-intestinal tract. A retrograde pyelo-ureterogram showed the left kidney and ureter to be normal. There was a complete duplication of the right ureter (fig. 1). Stereoscopic examination of the films localized the foreign object in the lower right renal pelvis. The renal function, as measured by indigo carmine, was normal from each kidney.

Surgical exploration revealed the foreign body to be a bobby pin in the lower pelvis of the right kidney. The pin was so corroded that it broke at the loop when attempt was made to remove it through the wall of the kidney pelvis. Following the operation, the child had no untoward reaction. She was discharged from the hospital on the third postoperative day. Two years after the operation, the patient was seen by one of us (C. W. D.). She was perfectly well.

DISCUSSION

After getting as complete a history as possible, urological study and removal of the pin, we do not know how the pin entered the kidney pelvis. There was no evidence that the pin had passed through any point in the skin. There has been no instrumentation of the bladder. At first we assumed that she had swallowed the pin, which had gone out from the duodenum into the kidney. However, after reviewing the literature we are in doubt that the pin came from the gastro-intestinal tract. Graves[1] and others report foreign bodies having migrated by reverse ureteric peristalsis from the bladder into the kidney pelvis.

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DIVERTICULUM OF THE URETER

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Diverticulum of the ureter is rare. In the past decade, the literature on this interesting entity has been extensively reviewed, the most outstanding contributions being made by Richardson in 1942 and Ormond S. Culp in 1947. The latter author presented an excellent review with illustrations and anatomical reproductions of the various types of anomalies reported in the literature as ureteral diverticula. From this report, it became quite evident that many of the cases reported as ureteral diverticulum were not acceptable as such; but instead represented ureterocele, segmental hydro-ureter, redundant hydronephrosis, or vesical diverticulum. The present authors, in accord with later writers, agree with Culp's new classification in that it establishes a more uniform method for categorizing future cases of this particular type of ureteral anomaly.

Ureteral diverticula are classified into two main groups: 1) congenital or "true" diverticula and 2) acquired or "false" diverticula. Culp defines the true diverticulum as "an ovoid or round extra-ureteral sac containing all the ureteral coats and communicating with the ureteral lumen through a distinct stoma." Although a blind-ending branch of a bifid ureter would by definition fall into the true diverticulum group, Culp prefers to list them separately and his reasons appear justifiable. As pointed out by Mayers (1949), however, no one would deny that both have the same embryological origin, that of multiple budding or premature cleavage of the ureteral anlage. "False" diverticula are thought to originate from a "blow out" or protrusion of the mucosa through the ureteral wall as a result of increased intra-ureteral pressure from various causes. By definition then, "false" diverticula contain incomplete, if any, muscular coats.

Of a total of 52 cases reported, Culp found only fifteen which conformed to his classification. (This is excluding 14 cases of blind-ending branches of bifid ureters.) Ten of these fifteen were congenital diverticula, to which he added one, and in 1949 Mayers added another bringing the total of congenital diverticula to twelve. To the 5 cases of acquired diverticula, Prat, Gahagan, and Fischman (1947) added another, and one which the present authors wish to add brings the total number of accepted ureteral diverticula to nineteen.

Several of the previously reported cases merit special mention. Rathbun's oft quoted case of single bilateral diverticulum is unique (1927). The diverticulum reported by Richardson in 1942 is the largest recorded, having a measured capacity of 3500 cc.

There are no pathognomonic symptoms. The patients are frequently found to have infected urine, with hydro-ureter and hydronephrosis to varying degree on the affected side. Pain in the flanks and/or lower abdomen is fairly common and

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These findings prove that foreign bodies may reach the right kidney either from the intestinal tract or through the ureter. In our patient there was no evidence, on surgical exploration, that the pin had perforated the kidney pelvis; therefore, we must conclude that the pin, in all likelihood, had ascended from the bladder through the ureter.

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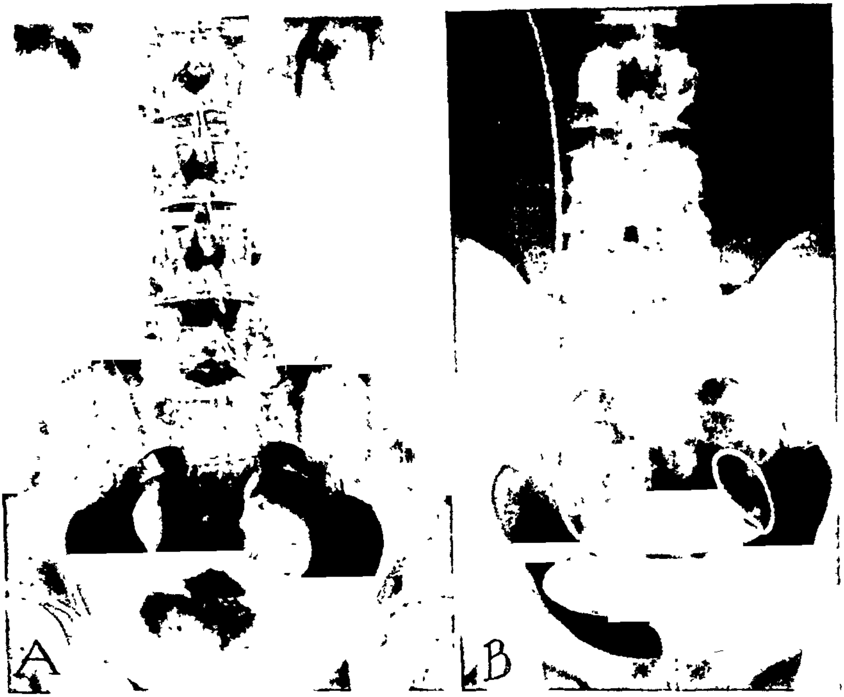

Fig. 1. *A*, excretory urography February 1948. Note fusiform dilatation of right lower ureter and left lower ureteral diverticulum. *B*, plain urogram with ureteral catheters in place (October 1951). Note development of large stone in lower right ureter. Catheter is coiled in left ureteral diverticulum which contains five small stones.

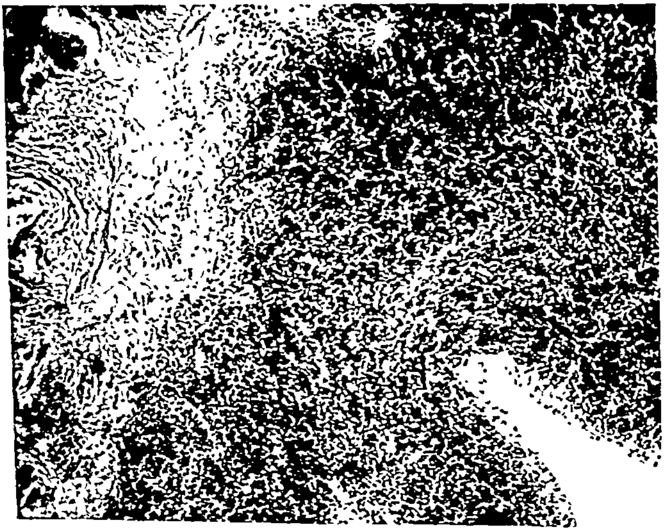

Fig. 2. Low power view of wall of diverticulum showing epithelial lining, underlying zone of hemorrhage and scattered smooth muscle bundles.

varies from a dull ache to severe colic. As one would expect, with urinary stasis and infection, calculi are fairly common.

Diagnosis is most often made by x-ray urography, the coiling of a ureteral catheter within the diverticulum being a fairly frequent finding.

Treatment, of course, depends upon 1) the size and location of the diverticulum, 2) the presence or absence of infection, and 3) the condition of the ureter and kidney above. Operative excision of ureteral diverticula may involve re-implantation of the ureter into the bladder, end to end ureteral anastomosis, nephroureterectomy, etc., depending upon the above mentioned factors. Also, in acquired diverticula, removal of the basic pathology responsible for the ureteral blowout is mandatory.

CASE REPORT

The patient (P. H. B.), a 38 year old white man, was first seen in August 1946, because of recurrent pyuria and difficulty in voiding. He gave also a history of intermittent low back and perineal discomfort over a period of several years. Urinalysis at that time was negative microscopically (patient had been placed on sulfa drug by his local physician 1 week previously), but prostatic smear was loaded with pus. He was treated conservatively with massage and sitz baths with temporary symptomatic improvement. In December 1946, however, he returned with a recurrence of symptoms and urinalysis revealed 30–40 white blood cells per high powered field. Urine culture yielded nonhemolytic staphylococcus. Sulfa drug and penicillin were begun and a week later the patient returned for excretory urography and cystoscopy. The urograms revealed a normal upper urinary tract, but there were saccular dilatations in the region of the vesicoureteral junction bilaterally. The details were obscured somewhat by a markedly dilated bladder. At cystoscopy, a median bar was found with moderate contracture of the vesical neck. The bladder contained 16 ounces of residual urine and the stoma of a bladder diverticulum was found in the region of each ureteral orifice. Attempts to catheterize both ureters were unsuccessful. The patient was subsequently admitted to the hospital and a transurethral resection of the median bar carried out. In February 1947, a bilateral vesical diverticulectomy was done through a cystotomy. The right ureteral orifice was found just within the diverticulum on that side necessitating severance of the right ureter and re-implantation. Recovery following both procedures was prompt and uneventful. The patient was then followed periodically with urethral and right ureteral dilatations. Symptomatic improvement was marked but the heavy pyuria continued intermittently. This cleared temporarily on several occasions with various antibiotics and urinary antiseptics.

In February 1948, excretory urography (fig. 1) revealed a diverticulum in the region of the lower left ureter and a fusiform dilatation in the right lower ureter. Surgery was advised but pressing business matters prevented the patient from consenting to surgery at that time. He was then given streptomycin over a period of 6 days which resulted in a dramatic clearing of his pyuria. The patient then moved to another city some ninety miles distant, was seen only once in 1949, and

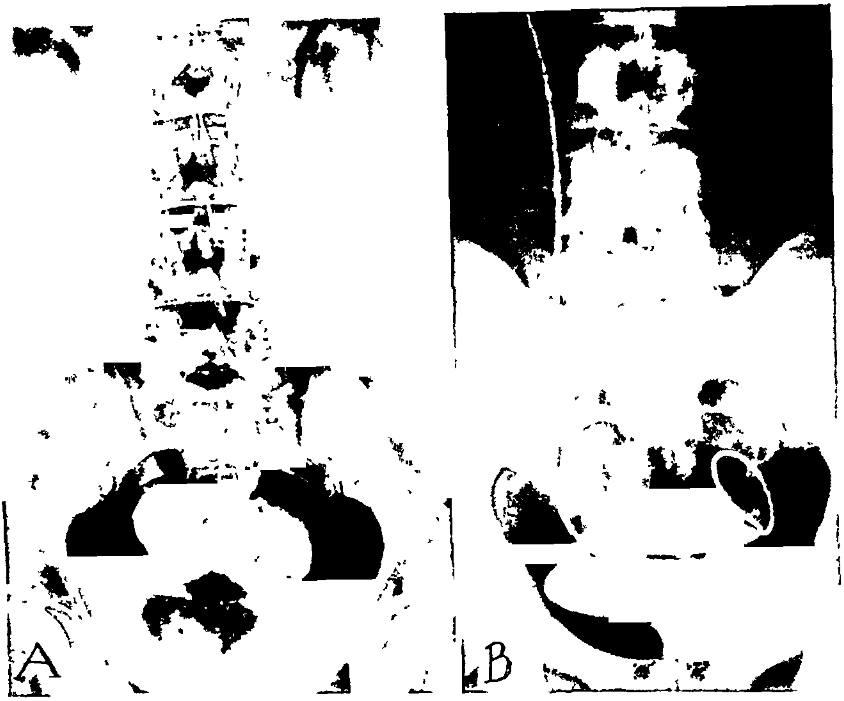

Fig. 1. *A*, excretory urography February 1948. Note fusiform dilatation of right lower ureter and left lower ureteral diverticulum. *B*, plain urogram with ureteral catheters in place (October 1951). Note development of large stone in lower right ureter. Catheter is coiled in left ureteral diverticulum which contains five small stones.

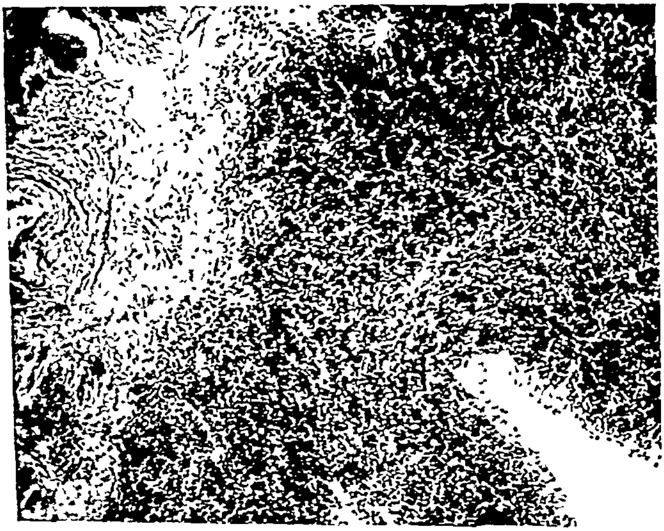

Fig 2 Low power view of wall of diverticulum showing epithelial lining, underlying zone of hemorrhage and scattered smooth muscle bundles

at that time was feeling fine and had completely negative urine. Pyelography was unchanged from that of a year previous. He then disappeared again and was not seen until October 1951, stating that he had been perfectly well until several months prior when he began having intermittent, sharp pain in the suprapubic region and distal urethra. Urography (fig. 1, *B*) revealed a large calculus in the lower right ureter and three to four smaller calculi in the diverticulum of the lower left ureter. The right ureteral calculus was causing moderate hydro-ureter and hydronephrosis on that side. Urinalysis, surprisingly enough, showed only occasional red and white blood cells. Surgery was again advised. On December 9, 1951 a right ureteral lithotomy and left ureteral diverticulectomy were performed through right and left modified Gibson incisions respectively. The diverticulum opened into the left ureter approximately one centimeter above the ureterovesical junction and had an estimated capacity of approximately fifteen milliliters. Recovery again was uneventful. All stones were calcium phosphate. Microscopically, the wall of the diverticulum was composed of a somewhat modified transitional epithelial lining with an underlying zone of hemorrhage. The outer layers were composed of scattered smooth muscle bundles and fibrous tissue (fig. 2).

DISCUSSION

Because of the incomplete muscular coats, this diverticulum is listed in the "acquired" group. There are two distinct possibilities as to etiology: 1) secondary to extra-ureteral pressure from the bladder diverticulum, and 2) secondary to operative trauma to the lower ureter when the bladder diverticulum was removed. The ureteral anomaly was first detected postoperatively but could easily have been present preoperatively and missed, since on the pyelograms the large bladder and bladder diverticula completely obscured the lower ureters. The patient has been seen several times since surgery and has remained completely asymptomatic. Excretory urography in February 1951 revealed a normal left upper urinary tract and almost complete regression of the right hydro-ureter and hydronephrosis.

ADDENDUM

Since the writing of this paper, another case of congenital diverticulum of the ureter has been reported (McGraw and Culp, March 1952). This was found in a 64 year old white woman who had presented herself because of a painless abdominal mass. At surgery, the corresponding kidney was found destroyed, and the large thin-walled diverticulum contained numerous calcified plaques. This brings the total number of authentic ureteral diverticula to twenty, thirteen congenital and seven acquired.

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THE COUDÉ ELLIK CATHETER FOR STONE EXTRACTION

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Our continued success with the Ellik catheter in the treatment of ureteral stones has caused us to accept it as the procedure of choice. On occasion, however, we have found it difficult or, rarely, impossible to pass the whistle-tip Ellik beyond the stone. This caused one of us (E. M. A.) to suggest the use of a Coudé catheter in such situations and a few were made up. At first they were utilized where difficulties were encountered with the standard Ellik with gratifying success. More recently, we have tended to use it as our choice over the whistle-tip type.

FIG. 1

Figure 1 shows the Coudé catheter looped about a stone. It forms an admirable dilating wedge. We believe this catheter can profitably be added to the armamentarium of the urologist.

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ELECTROCYSTOGRAPHY: A STUDY OF BLADDER CONTRACTIONS MEASURED BY DIFFERENCES OF ELECTROPOTENTIAL

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In an attempt to develop a clinical method of studying and diagnosing lesions of the bladder, a means of recording electropotential variation in the muscle of the urinary bladder is being investigated.

Medicine today makes use of electrocardiograms to aid in diagnosing heart lesions, and electro-encephalograms in the study and diagnosis of lesions of the brain. Why not, therefore, use a similar method in the diagnosis of lesions of the bladder?

Although cystometry is a useful method for studying the normal and the pathological physiology of the bladder, it has not proved reliable as a diagnostic procedure.[1] Extensive study reveals that there is a great variability of cystometrograms in the three groups: normal, hypertonic, and atonic. Also that, by cystometry, one group is not differentiated from the other and that there is a broad overlap of the pathological and normal.[1] The generally accepted statement that the cystometrogram is useful in distinguishing between a neurogenic bladder and a bladder affected by an obstructive lesion is not true. There is nothing distinctive in the cystometric curve to distinguish the myogenic from the neurogenic bladder. The atonic neurogenic bladder produces cystometric findings identical with those of a decompensated obstructed bladder. The shortcomings of cystometry as a diagnostic procedure has been established.[1]

Investigators at the University of Virginia[2] utilized a Grass electro-encephalograph to record differences of electro-potential between two bare electrode tips thrust blindly into the bladder. They obtained a characteristic wave pattern (fig. 1). The "bladder waves" occurred every 2.3 minutes and lasted for 1.3 seconds. It is believed that these waves of vesical contraction can be recorded by measuring differences of electrical potential.

In the present study the same type of Grass electro-encephalogram machine was used. The bladder waves recorded had a pattern and frequency similar to those of the Virginian workers (fig. 2, *1*). In addition to substantiating this earlier study, this subsequent work has shown that extravesical influences do not cause the "bladder waves" and has revealed the effect of parasympathetic stimulus on the waves recorded.

METHOD

Muscle contraction is accompanied by the passage of an electrical wave along the muscle, which can be measured as a difference of electrical potential between

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[1] Weyrauch, H. M., Eschscholtzia, L. L. and Howard, Joan: The failure of the cystometrograms as a diagnostic test. J. Urol., 51: 191–209, 1944.

[2] Corey, E. L., Boyce, W. H., Vest, S. A. and Franch, C. R.: Electro-potential changes in human urinary bladder: A method of measurement. J. Applied Physiol., 3: 631–636, 1951.

any two separated locations of the muscle. Excitation and conduction occur in both smooth and striated muscle,[3] and the electro-potentials of smooth muscle have been studied extensively.[4, 5, 6, 7, 8, 9] However, until recently no work has been done on electrical changes in bladder muscle. In this study all work was done on the urinary bladder in man. The subjects were men between 40–60 years of age who had no bladder disease. To measure minute differences in potential occuring in the bladder two insulated McCarthy fulgurating electrodes, having needle points (fig. 3) were passed into the bladder through a Brown-Buerger catheterizing cystoscope during the course of cystoscopic examination. Under direct vision, the pointed electrodes were thrust into the bladder muscle at the same location for each test, one on each side at a point 1 cm. above and 1 cm. medial to the respective ureteral orifice. The electrodes were then connected to one channel of a Grass electro-encephalograph and recordings were taken with the bladder slightly distended with approximately 200 cc of water. During various phases of the study other channels of the electroencephalograph were used to record electrocardio-

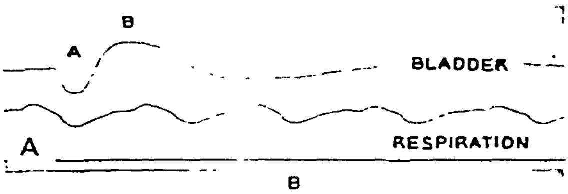

FIG. 1. Bladder waves recorded by University of Virginia group[2]

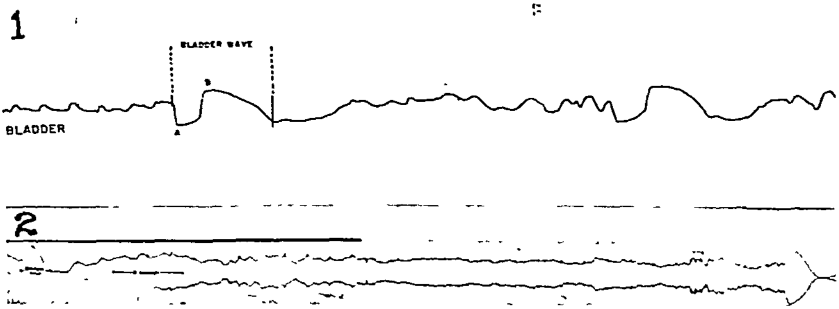

FIG. 2. *1*, Characteristic bladder waves. In order to show two consecutive waves clearly, 60 second interval between two waves has been omitted. *2*, Complete cycle from one bladder wave to succeeding wave. Waves are occurring at 86 second intervals.

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[3] Rosenblaeth, Arturo: Conduction in smooth muscles. Biol. Symp., 3: 111–120, 1941.

[4] Bozler, Emil: Action potentials and conduction of excitation in muscle. Biol. Symp., 3: 95–110, 1941.

[5] Bozler, Emil: An analysis of the properties of smooth muscle. Col. Spr. Harb. Symposia, 4: 260–266, 1936.

[6] Bozler, Emil: Reflex peristalsis of the intestine. Am. J. Physiol., 157: 338–342, 1949.

[7] Bozler, Emil: Action potentials accompanying conducted responses in visceral smooth muscles. Am. J. Physiol., 136: 553–560, 1942.

[8] Bourdillon, R. B.: Vaginal potentials in rabbits. J. Physiol., 97: 138–152, 1939.

[9] Bourdillon, R. B., and Lidwell, O. M.: Slow vaginal potentials. J. Physiol., 98: 480–486, 1940.

grams, abdominal muscle movement, and respiratory movement. In addition, recordings were made of various phases of vesical activity such as emptying and filling.

OBSERVATION AND RESULTS

After standardizing a method, electropotential changes in the normal bladder were recorded. These tracings were named electrocystograms. The recordings revealed waves of characteristic pattern (fig. 2, *1*); these waves occurred approximately every 2.3 minutes and lasted approximately 1.3 seconds. Note the similarity of these waves to those recorded by the University of Virginia workers (fig. 1).

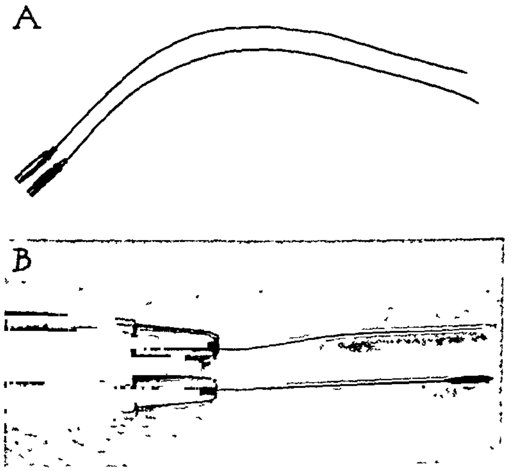

FIG. 3. *A*, McCarthy fulgurating electrodes used in study. *B*, enlargement of electrodes showing contact end of electrodes. Note needle pointed tips.

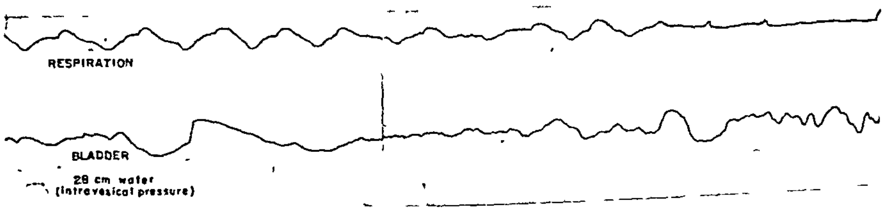

FIG. 4. Bladder wave and simultaneous waves of respiratory movement

In order to present two consecutive bladder waves clearly in one picture the waves have been brought together, eliminating a time interval of 60 seconds. Figure 2, *2* illustrates a complete cycle from one bladder wave, through a "resting period" to the onset of another bladder wave; these waves were spaced at 86 second intervals.

The next step was to record electrocystograms and respiratory movements simultaneously, utilizing a thermocouple at the nose. This was done to determine whether respiratory movement was the cause of the production of the bladder

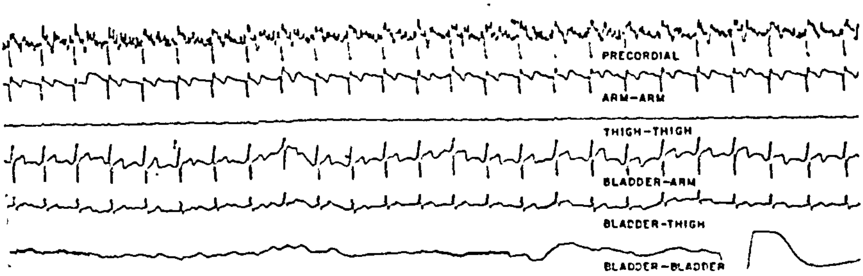

FIG. 5. Simultaneous record of bladder waves and possible extravesical influences: heart, arm, thigh.

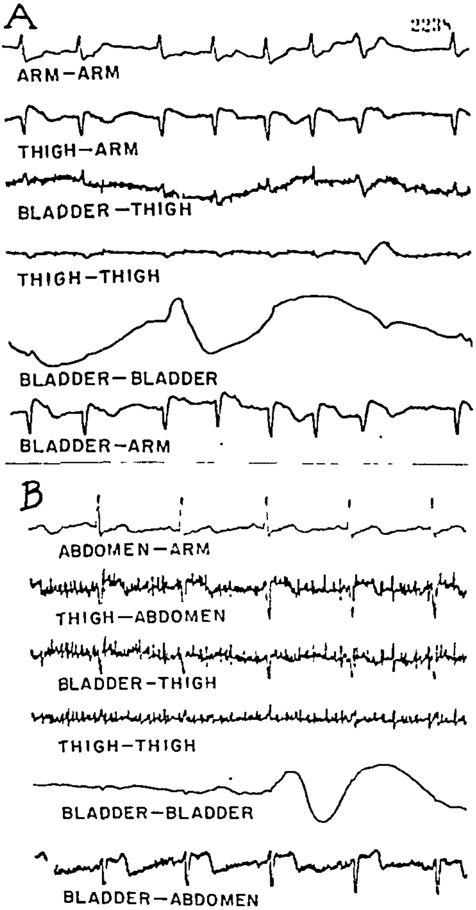

FIG. 6. *A*, simultaneous record of bladder waves and possible extravesical influences: arm, thigh. *B*, simultaneous record of bladder waves and possible extravesical influences: abdominal muscles, arm, thigh.

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OBSERVATION AND RESULTS

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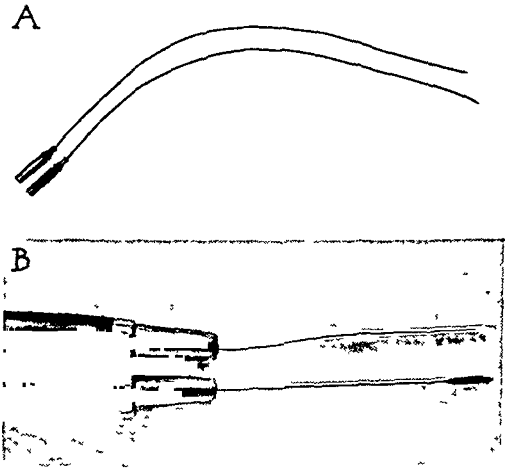

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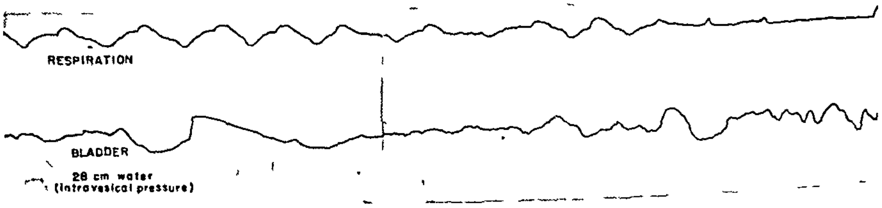

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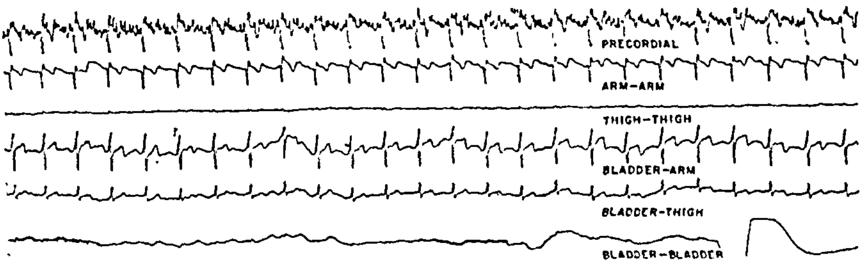

FIG. 5. Simultaneous record of bladder waves and possible extravesical influences: heart, arm, thigh.

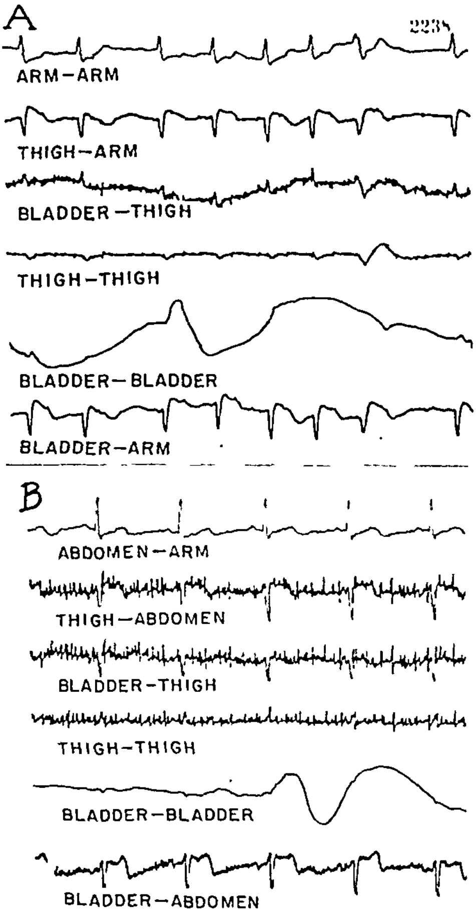

FIG. 6. *A*, simultaneous record of bladder waves and possible extravesical influences: arm, thigh. *B*, simultaneous record of bladder waves and possible extravesical influences: abdominal muscles, arm, thigh.

waves. Figure 4 illustrates that the bladder waves are independent of respiratory movements.

The question then arose, do these recorded bladder waves reflect vesical contraction or are they artefacts produced by extravesical influences? In order to answer this question electropotentials registering muscle movement from the bladder, abdominal wall, and the extremities were simultaneously recorded. In addition, recordings from a precordial lead were taken. These records (figs. 5, 6 and 7) well illustrate that bladder waves pictured in the electrocystogram are characteristically independent of extravesical influences.

Additional study was then initiated to determine the effect of parasympathetic stimuli on the bladder, by means of electrocystograms. Figure 6 illustrates the bladder waves obtained 20 minutes after the intramuscular injection of prostigmine (1 ml of a 1:2000 dilution). The bladder waves occurred every 10 to 25 seconds rather than every 86 seconds (fig. 8). Upon parasympathetic stimulus the bladder waves do not change their force or configuration but they are more frequent.

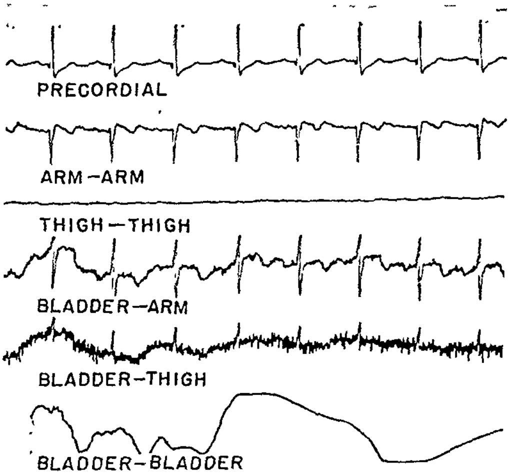

FIG. 7. Simultaneous record of bladder waves and possible extravesical influences: heart, arm, thigh.

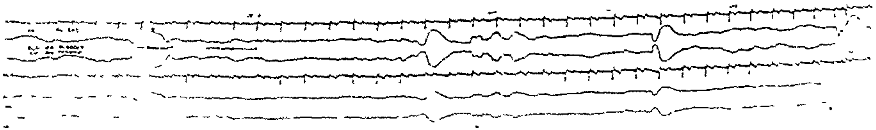

FIG. 8. Record of bladder waves after administration of parasympathetic stimulant

DISCUSSION

The observations illustrated lend support for the hope that a method of recording vesical activity, by virtue of changes in electropotential, has been devised. Further, the experimental data presented seem to allow the assumption that the bladder waves (electrocystograms) represent vesical activity and are not produced by extravesical influence.

Whether electrocystography will prove useful as a diagnostic measure is still not known. Studies are now being carried out at Stanford University to provide further evidence that electrocystograms indicate bladder contractions. Additional studies are to be instituted to determine the electrocystographic patterns of abnormal bladders in order to critically evaluate electrocystography as a diagnostic test.

SUMMARY

A new approach to studying the bladder is being investigated. The activity of the bladder can be recorded in electrocystograms. These bladder waves apparently occur independently of extravesical influences and are affected by parasympathetic stimulation of the bladder.

The author wishes to thank Doctor Henry M. Weyrauch of Stanford University for his encouragement and help during the course of this study.

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THE EFFECT OF BANTHINE IN THE TREATMENT OF GENITO-URINARY DISORDERS

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From the Second Cornell Surgical (Urology) Division, Bellevue Hospital and The Departments of Medicine and Surgery (Urology) Cornell University Medical College, New York, N. Y.

The action of Banthine on the gastro-intestinal tract has been the subject of extensive investigation.[1-6] Fifty to one hundred milligrams administered by mouth have been shown to counteract the effects of parasympathetic stimulation. When opposing stimuli are not too strong, Banthine may reduce gastric acid production and motor activity and inhibit peristaltic contraction of the small intestine and colon. [7, 8] Urinary retention has been observed during the course of Banthine administration. For this reason we decided to investigate the effects of this drug on the urinary tract.

METHODS OF INVESTIGATION

The present report covers observations of the effects of Banthine on the urinary bladder and includes a preliminary statement of observations on the renal pelvis and ureter.

This group included some with normal, and some with abnormal, bladders. Banthine was administered by mouth in single doses of 100 mg. or 150 mg., or in repeated doses of 50 to 100 mg. four times a day over a period of several weeks. Observations were also made following intramuscular injections of 25 or 50 mg. Control observations were made with a bitter placebo of identical

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Supported by a grant from the Searle Company.

Read at annual meeting, American Urological Association, Atlantic City, N. J., June 25, 1952.

[1] A. Longino, F. H., Grimson, K. S., Chittum, J. R. and Metcalf, B. H.: An orally effective quaternary amine, banthine, capable of reducing gastric motility and secretions. Gastroenterology, **14**: 301, 1950.

B. Grimson, K. S., Lyons, C. K. and Reeves, F. J.: Clinical trial of banthine in 100 patients with peptic ulcers. J. A. M. A., **143**: 873, 1950.

C. Comments: A clinical trial of banthine in cases of peptic ulcer. Gastroenterology, **14**: 583, 1950.

[2] Smith, C. A., Woodward, E. R., Janes, C. W. I. and Dragstedt, L. R.: The effect of banthine on gastric secretions in man and experimental animals. Gastroenterology, **15**: 718, 1950.

[3] Benjamin, F. B., Rosiere, C. E. and Grossman, M. I.: A comparison the effectiveness of banthine and atropine in depressing gastric acid secretions in man and dog. Gastroenterology, **15**: 727, 1950.

[4] Brown, C. H. and Collins, E. N.: The use of banthine in the treatment of duodenal ulcer. Gastroenterology, **18**: 26, 1951.

[5] Plummer, K., Burke, J. O. and Bradford, S. C.: The effect of methantheline bromide (banthine) on the insulin induced secretion of gastric acid, mucoproteose and mucoprotein; Physiological implications; Gastroenterology, **18**: 218, 1951.

[6] Abbot, F. K., Mack, M. and Wolf, S.: The action of banthine on the stomach and duodenum of man with observations on the effects of placebos. In press.

[7] Kern, F., Almy, T. P. and Stolk, N. J.: An experiment and preliminary clinical study of the effect of a new quaternary amine, Banthine, upon the human colon. Gastroenterology, **17**: 198, 1951.

[8] Kern, F. Jr., Almy, T. P. and Stolk, N. J.: Effects of certain antispasmodic drugs on the intact human colon with special reference to Banthine (b-diethylaminoethyl xanthene-9-carboxylate methobromide.) In press.

appearance to Banthine, or by sterile hypodermic injection, as well as without the administration of any agent.

Observations on the tone and capacity of the bladder were made with an ordinary water cystometer. Physiological saline was introduced into the empty bladder slowly to avoid rapid abnormal distention of the bladder and consequent reflex contraction. The time of appearance of the desire to void, and of the presence of pain were noted. Experiments in which single oral dosage of Banthine was used were carried out as follows: After the bladder capacity had been established, the contents of the bladder were withdrawn and measured. The patient was then given 50 or 100 mg. Banthine orally. The cystometric determination was then repeated at 30 minute intervals after the ingestion of Banthine or placebo.

This technique was altered somewhat in the experiments in which intramuscular or subcutaneous injections were given. After the bladder had been emptied it was filled slowly to near capacity and the inflow clamped off. Readings, obtained directly from the water manometer, were taken every minute until the conclusion of the experiment. During a preliminary ten to twenty minute "control" period, observations were made of pulse rate, pupillary accommodation, sensation of bodily coolness or warmth, perspiration, salivation, presence or absence of desire to void, and the patient's general mental state. The injection was then administered and the above observations were continued until the termination of the experiment. The contents of the bladder were then withdrawn and measured.

Other subjects were studied while on a maintenance dose of 100 mg. Banthine, four times a day. In the early experiments cystometric determinations were carried out daily on these subjects. Later, because of the possibility that repeated distention of the bladder with fluid might cause some relaxation and give a false impression of the effects of the drug, the cystometric determinations were done only twice a week. The bladder capacity was determined by either of the foregoing methods described. After a variable number of days these patients were given the placebo instead of Banthine and then given Banthine again without knowing that the medication was being changed. Further controls were obtained by day to day measurement of bladder capacity without any agent being given.

RESULTS

Oral administration of single doses. Twenty-seven separate experiments were performed on three subjects with reduced bladder capacity, and three with normal bladder capacity. Each was given 100 mg. Banthine by mouth while the bladder capacity was being measured repeatedly. Although variable in degree, the results in both groups were relatively uniform. When the original capacity was as great as 250 cc there was rarely an increase in the capacity of more than 100 cc. The greatest effects were observed with bladder capacity of less than 200 cc. The effects of 100 mg. Banthine compared with placebo are shown in figure 1, *A*. Within 30 minutes after administration bladder capacity in most instances was observed to increase. Maximum effect was observed in the neighborhood of 75 minutes and within 3 to 4 hours the effects had largely subsided.

Intramuscular administration of single doses. Thirteen observations were made on 3 patients with normal bladders and 2 patients with hypertonic bladders who were given 50 mg. Banthine or saline as a placebo. Again, the most striking effects were observed in those subjects who had the smallest bladder capacity and the highest intracystic pressure during the control period (fig. 1, *B*).

Repeated doses. In order to establish a control group, 10 individuals with apparently normal bladders were given 100 mg. Banthine four times a day. Four of these individuals displayed an increase in bladder capacity varying from 20 to 47 per cent while they were taking Banthine. The remaining six showed an increase from 3 to 16 per cent which we do not consider significant. A comparison of the effects of Banthine and placebo in the case of one such subject is shown in figure 2, *A*.

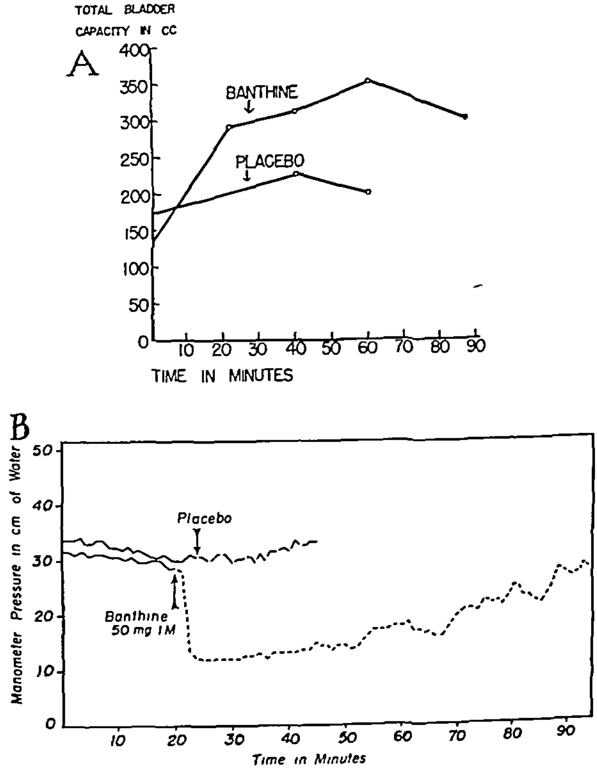


FIG. 1. *A*, comparison of effects of single oral dosage of Banthine and placebo on bladder capacity in 50 year old woman with hypertonic bladder. *B*, cystometric tracing in a 60 year old man with hypertonic bladder. 200 cc of saline was introduced at start of experiment and 340 cc of fluid was present at end of experiment.

Fourteen subjects with urinary incontinence, varying from a mild stress-incontinence to a total inability to retain urine were observed. Ten of these patients were males, and four were females. As in the normal subjects, the bladder capacity was increased but there was no significant change in the amount or degree of stress incontinence.

Six patients who were hospitalized because of chronic cystitis were included in this study. The bladder capacity of each was doubled while taking Banthine.

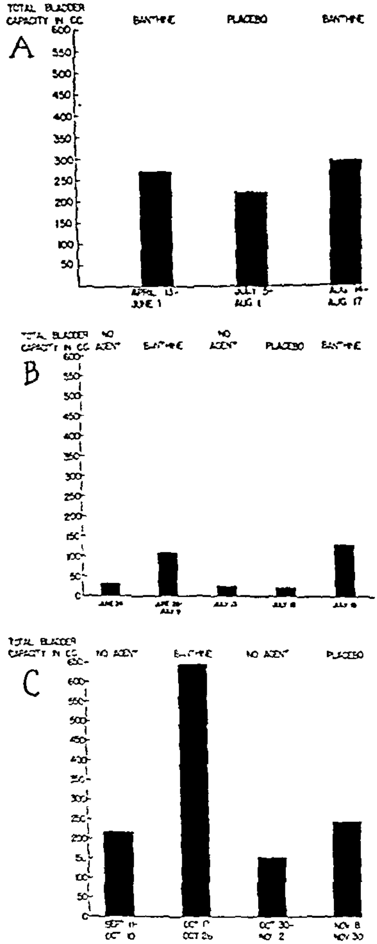
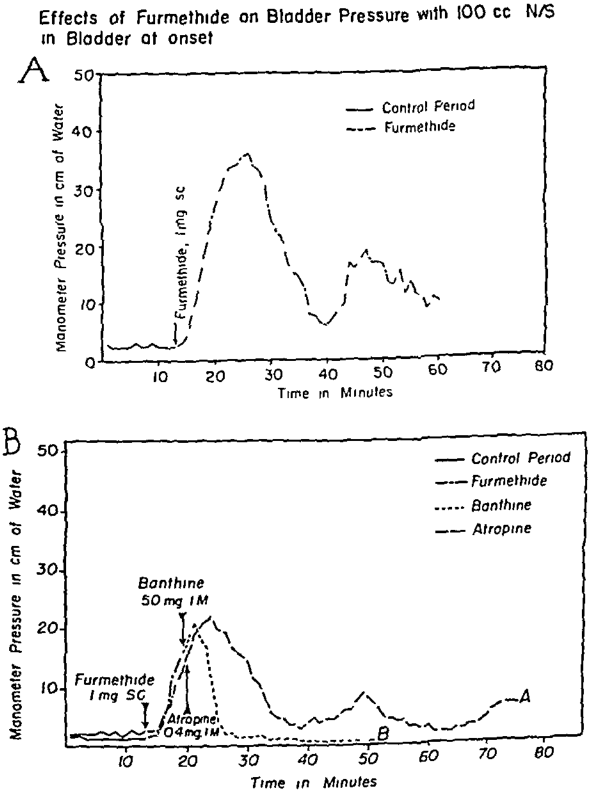


FIG. 2. *A*, comparison of effects of maintenance dosage of Banthine and placebo on bladder capacity in a 56 year old man with normal bladder. *B*, comparison of effects of maintenance dosage of Banthine and placebo on bladder capacity in 73 year old man with chronic cystitis and greatly reduced bladder capacity. *C*, comparison of effects of maintenance dosage of Banthine and placebo on bladder capacity in 46 year old woman with advanced multiple sclerosis.

Examples of the effects noted are shown in figure 2, *B*. These patients improved rapidly with a prompt decrease in urgency and frequency of urination. Six ambulatory patients suffering from chronic cystitis were given the same quantities of Banthine without significant improvement in the symptoms of frequency and urgency of urination. It is possible that larger doses of Banthine would have reduced the symptoms of the individuals who were dealing with the day-to-day stresses of life outside of the hospital.

Four patients with disease of the upper motor neurons, multiple sclerosis, paraplegia, hemiplegia, and cerebral arteriosclerosis were given the maintenance dose of Banthine. All showed substantial increase in bladder capacity. The changes observed in one of these are shown in figure 2, *C*.

Four women with chronic recurrent Hunner ulcers were observed, and they all showed decrease in symptoms while taking Banthine. These patients have not been under observation long enough to determine the permanence of results.



Effects of Furmethide on Bladder Pressure with 100 cc N/S in Bladder at onset

FIG. 3. *A*, increased in contractile state of hypertonic bladder following administration of furmethide. *B*, prompt interruption of furmethide effect by Banthine (dotted line). Atropine effect slower and less complete (broken line).

Four children with enuresis were given 50 mg. Banthine at bedtime. In all four, urinary symptoms disappeared completely. However, Zufall[9] who treated twelve enuretic adults in the Army, found no improvement after Banthine. One private patient in whom enuresis developed following a suprapubic prostatectomy lost the enuresis after taking 100 mg. Banthine at bedtime.

Eleven subjects were observed who had complaints of frequency of urination associated with chronic emotional distress without any demonstrable defect in the bladder dynamics. Cystoscopic examination of each patient revealed an entirely normal bladder and urethra. Cystometric determinations were normal. Only one individual showed a significant decrease in symptoms while on Banthine therapy.

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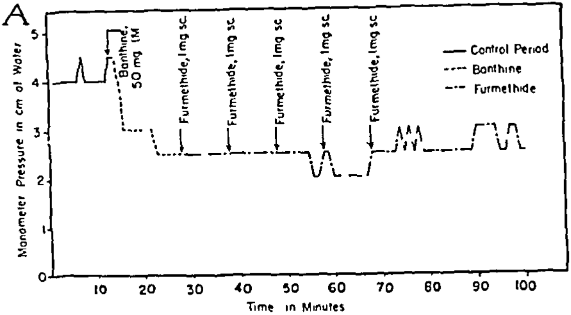
[9] Zufall, Robt. Lt., AUS: Personal communication.

Eighteen patients with bladder spasm following prostatectomy were given Banthine, 100 mg. four times a day. Fourteen of these patients, whose symptoms were not severe, were improved. However, the remaining 4 patients with severe postoperative bladder spasm failed to obtain any relief from this amount of Banthine.


Effects of Banthine followed by five separate injections of Furmethide, each 1 mg sc., on Bladder Pressure with 100 cc N/S in Bladder at onset

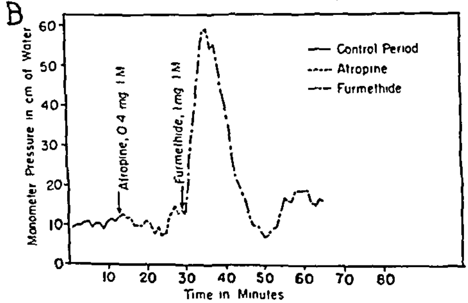
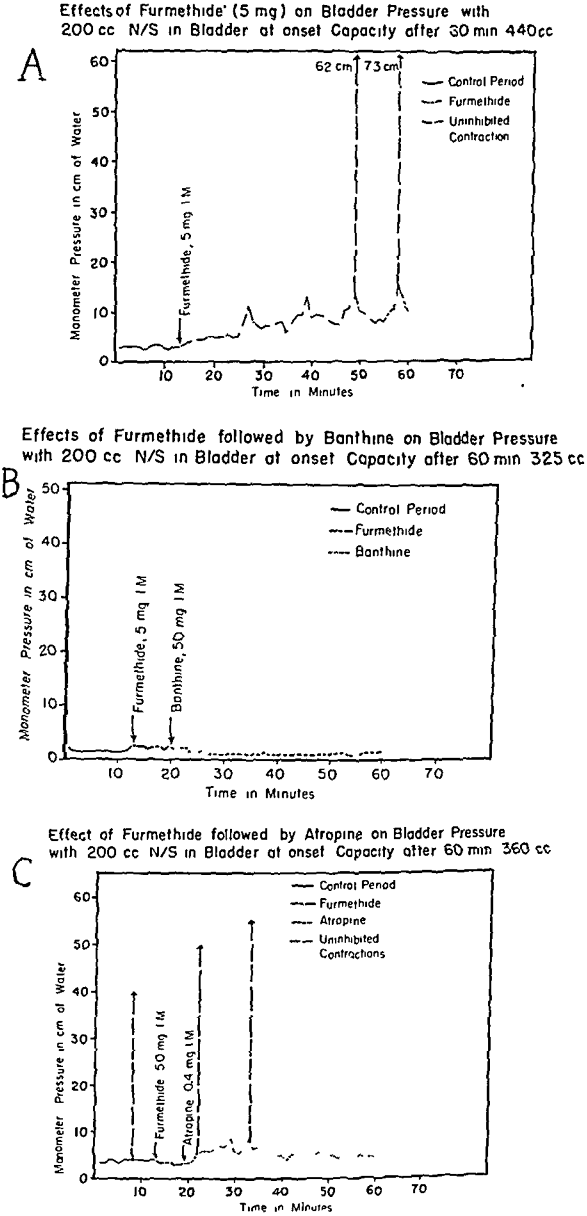

Effect of Atropine followed by Furmethide on Bladder Pressure with 100 cc N/S in Bladder at onset Capacity after 65 min 280 cc.

FIG. 4. *A*, failure of Furmethide to increase contractile state of bladder inhibited by Banthine. Patient same as figure 3,*A*. *B*, failure of atropine to counteract effect of Furmethide.

Side effects. Most of the subjects noted dry mouth and difficulty in focussing the eyes while taking 100 mg. of Banthine four times a day. In one subject, 50 mg. Banthine given intravenously produced marked increase of pulse rate from 78 to 150 and the blood pressure from 130/80 to 180/100.

EFFECT OF BANTHINE ON HYPERTONUS OF THE BLADDER INDUCED BY PARASYMPATHOMIMETIC DRUGS

The procedure in these experiments was identical with those in which parenteral Banthine alone was administered with the exception that the bladder



Effects of Furmethide' (5 mg) on Bladder Pressure with 200 cc N/S in Bladder at onset Capacity after 30 min 440cc

Effects of Furmethide followed by Banthine on Bladder Pressure with 200 cc N/S in Bladder at onset Capacity after 60 min 325 cc

Effect of Furmethide followed by Atropine on Bladder Pressure with 200 cc N/S in Bladder at onset Capacity after 60 min 360 cc

FIG. 5. *A*, weak stimulating effect of Furmethide on normal bladder. *B*, blocking of Furmethide effect on normal bladder by Banthine. Patient same as *A*. *C*, incomplete blocking of Furmethide effect on normal bladder by atropine. Patient same as *A*. Note uninhibited contractions.

was filled to 20 to 25 per cent of capacity. Three subjects with hypertonic bladders were given 1 to 2 mg of Furmethide* subcutaneously or intramuscularly. *Within* 3 to 15 minutes there occurred a brisk increase in the contractile state of the bladder with an intense desire to void (fig. 3, *A*). The effect of the Furmethide was maximum in 15 to 17 minutes, and had largely subsided in 35 to 40 minutes. Injection of 50 mg. Banthine intramuscularly at any time during the course of this response promptly interrupted it so that the pressure was restored to its original levels or lower, within 5 to 10 minutes, and the desire to void was eliminated. This experiment was repeated twice using 0.4 mg. atropine for the purpose of comparing the efficacy of Banthine and atropine. In each case however, the response was slower and less complete than was noted with Banthine (fig. 3, *B*).

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* Smith Kline and French brand of furthethonium iodide supplied by the manufacturer.

In two experiments, Banthine was given first. During the next 70 minutes, injection of 1 mg. Furmethide on five separate occasions failed to induce an increase in the contractile state of the bladder, or any desire to void (fig. 4, *A*). In two further experiments, injection of 0.4 mg. atropine was followed by a 1 mg. injection of Furmethide. This dosage was sufficient to interrupt the atropine effect with an accompanying increase in bladder pressure and an intense desire to void (fig. 4, *B*). Two placebo experiments were performed using 2 cc saline and no effect was observed. Two subjects with normal bladders were studied in the same manner. Five milligram injections of Furmethide were required to cause any appreciable increase in bladder pressure, or desire to void (fig. 5, *A*). A 50 mg. injection of Banthine was sufficient to counteract, or prevent, the action of the Furmethide (fig. 5, *B*), but 0.4 mg. injection of atropine was not sufficient to accomplish this completely (fig. 5, *C*). Experiments were performed using 2 cc saline as a placebo as well as experiments involving no medication, but no change in intracystic pressure was observed.

Ureter and kidney pelvis. Attempts to measure and record contractile activity in the ureter and kidney pelvis and to estimate the effects of Banthine on these structures were made using Trattner's hydrophorograph.[10] This instrument was not well suited to the problem because the recording is dependent upon volume of urine flow as well as contractile activity of the ureter. At present the studies are being pursued with the use of an electrical transducer and an electronic device, which records intra-ureteral pressures independent of urine flow.

Excretory urograms were taken of five normal subjects. Several days later a second series was done after pre-medication with Banthine, 150 mg. given by mouth 30 minutes before the intravenous injection. In both series determinations were kept as similar as possible. No significant difference in the density of contrast medium could be determined by x-ray.

Fifteen patients with renal colic due to calculi were treated with Banthine. The results suggest that it is useful, but a larger series will be necessary to establish this conclusion.

SUMMARY AND CONCLUSIONS

The effects of Banthine on the function of the urinary bladder have been investigated in 74 patients with various bladder disorders, and in seventeen normal subjects. Over five hundred cystometric determinations have been carried out. In general, there appeared to result a decrease in bladder tone, associated with diminished force and frequency of spontaneous contractions. This resulted fairly uniformly in an increase in bladder capacity. The effect was most striking in patients with contracted bladders and bladders of small capacity. In these subjects, nocturia, diuria, and strangury could be reduced with minor side-effects of the drug. In the absence of excessively strong stimuli, Banthine has been shown to relax bladder spasms caused by parasympathetic stimulation. It has been found that Banthine is a better antagonist to Furmethide than atropine in the dosage used in these experiments. Preliminary observations on the effect of Banthine on the renal pelvis and ureter have been reported.

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[10] Lapides, J.: The physiology of the intact human ureter. J. Urol., 59: 501, 1948.

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PLASTIC SURGERY ON THE URINARY BLADDER

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The urinary bladder is admirably adapted to plastic surgery. Its blood supply is profusely anastomosing, the muscle bundles of its wall are interlacing and the mucosa is not delicate.

This report covers the following plastic surgical procedures which we have done on the urinary bladder of experimental animals and/or of patients:

1) Reconstruction of lower segment of ureter.
2) Construction of suprapubic spigot for permanent cystostomy.
3) Reconstruction of urethra with tube made from a bladder flap.
4) Re-inforcing bladder wall by overlapping to reduce size and increase tone of bladder.
5) Anastomosis of isolated loop of sigmoid to bladder to enlarge its capacity.
6) Transplantation of trigone to sigmoid.

REVIEW OF LITERATURE

The reconstruction of the lower segment of the ureter by a tube made from a bladder flap has been successfully performed both experimentally on animals, and clinically in human subjects.[1, 2, 3, 4, 5, 6, 7, 8] The most recent report gave a 5-year follow-up in the case of a ureterovaginal fistula in which the ureteral defect was repaired by use of a tube made from a bladder flap. There was no evidence of ureteral obstruction and there was a definite regression of the previous hydronephrosis as shown by pyelography.

The use of a bladder flap in the reconstruction of the urethra has been reported recently by two of the authors.[9] Previous to this, Markoff in 1928 reported a case of vesicovaginal fistula with complete destruction of the urethra. A new urethra was formed by incising the bladder anterior to the fistula and pulling the bladder out to form a new urethra. The vesicovaginal fistula was then closed,

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Read at annual meeting. American Urological Association. Atlantic City, June 26. 1952.

[1] Baiden, A.: Demel autoplasty of ureter with aid of bladder in man. Zentralbl. f. gynak., 54: 3237–3239, 1930.

[2] Barnes, R. W. and Farley, S. E.: Reconstruction of lower segment of ureter with tube made from bladder flap; preliminary report. J. Urol., 59: 466–470, 1948.

[3] Demel. R.: Plastic construction of ureter from bladder. Zentralbl f. chir., 51: 2001–2008, 1946.

[4] Flocks, R. H.: Ureterovesical anastomosis when proximal ureter is short. Canad. Med. J., 55: 514–516, 1946.

[5] Ockerblad, N. F.: Re-implantation of ureter into bladder by flap method. J. Urol., 57: 845–847, 1947.

[6] Ockerblad, N. F. and Carlson, H. E.: Ureterovaginalfistula. J. Urol., 42: 263–268, 1939.

[7] Rhode, C.: Replacement of portion of ureter by tissue from bladder. Zentralbl. f. chir., 64: 409–412, 1937.

[8] Spies, J. W., Johnson, C. E. and Wilson, C. S.: Reconstruction of ureter by means of bladder flaps. Proc. Soc. Exper. Biol. & Med., 30: 425–426, 1932.

[9] Barnes, R. W. and Wilson, W. M.: Reconstruction of urethra with tube made from bladder flap. Urol. & Cutan. Rev., 53: 604–605, 1949.

producing a satisfactory result. It was concluded that "a destroyed urethra can be replaced by an artificial urethra formed with the bladder wall."[10]

Many other techniques have been suggested to replace the completely destroyed urethra.[91–9] In 1863, Baker Brown perforated the anterior wall of the vestibule below the clitoris with a trocar and made a puncture wound into the bladder. A silver catheter was placed and eventually the wound healed with a continent urethra. Others have used tunnels made from vaginal and labial flaps, but restoration of urinary continence following these procedures has not been frequent. In order to improve control, the construction of an artificial sphincter by using levator ani muscles, the gracilis muscle, and the pyramidalis muscle has been tried. The results in most of these were not encouraging.

The plastic reconstruction of a major portion of the floor of the bladder in an obstetrical case was accomplished by the use of vaginal flaps.[13]

Pedicled flaps from the bladder wall were used in the repair of scrotal hypospadias by Zeller in Germany in 1935 with an excellent result.[19]

The use of an isolated intestinal loop to enlarge the capacity of the bladder was tried by Seberring in 1932. A portion of the ileum was anastomosed to the bladder in the experimental animal. The follow-up revealed apparently normal bladder function and a normal nonprotein nitrogen.[20] More recently Couvelaire has successfully enlarged the bladder by anastamosing an isolated segment of large bowel.[21]

The formation of an artificial urinary bladder by using isolated segments of intestine has been reported by many authors. Notable results have been obtained by the use of the isolated cecum with the attached ileum as urethra. Even the gallbladder has been tried in the experimental animal, with terminal uremia as the result of mucosal absorption.[20–24]

[10] Markoff, N.: New method for restoration of female urethra by formation with bladder in cases of complete destruction. Gynec. et Obst., **18:** 6–17, 1928.

[11] Caughlan, G. V.: Ureterovaginal fistula: Repair of urethral defect by use of bladder flap. J. Urol., **58:** 428–430, 1947.

[12] Deming, C. L.: Transplantation of gracilis muscle for incontinence of urine. J.A.M.A., **86:** 822–823, 1926.

[13] Gomoiu, V.: Plastic reconstruction of urethra in woman by flap formation. Wien. med. Wchnschr., **90:** 524–525, 1940.

[14] Harris, S. H.: Reconstruction of female urethra. Surg., Gynec. & Obst., **61:** 366–368, 1935.

[15] Marion, G.: Construction of continent urethra in female; application in exstrophy of bladder. J. d'urol., **37:** 393–402, 1934.

[16] McGaw, W. H.: Restoration of female urethra and vesical sphincter; operative technique resulting in urinary control. Surg., Gynec. & Obst., **47:** 408–412, 1928.

[17] Rosser, C. M.: Transplantation of vermiform appendix into female bladder to supply absent urethra. Ann. Surg., **69:** 435, 1919.

[18] Ward, G. G.: Reconstruction of urethra after complete loss, complicating an extensive vesicovaginal fistula, operative technique employed with success. Surg., Gynec. & Obst., **37:** 678–682, 1923.

[19] Zeller, O.: Replacement of missing urethra in patient with scrotal hypospadias by pedicled flaps from bladder wall; case. Med. Welt., **9:** 565–567, 1935.

[20] Seberring, W.: Use of isolated intestinal loop to enlarge capacity of bladder; clinical and experimental study. Proc. Staff Meet. Mayo Clinic, **7:** 123–127, 1932.

[21] Couvelaire, R.: La petite vessie; des tuberculeux genito-urinaires essai de classification place et variantes des cysto-intestino-plastics. J. d'urol. **56:** 381, 1950.

[22] Lay, E. Bussa: Bladder made from gallbladder. Arch. ital. di chir., **11:** 333–359, 1925.

[23] Merricks, J. W., Gilchrist, R. K., Hamblin, H. and Reiger, I. T.: A substitute bladder and urethra using cecum as bladder and ileum as urethra. J. Urol., **65:** 581–589, 1951.

[24] Rubin, S. W.: The formation of an artificial urinary bladder with perfect continence; an experimental study. J. Urol., **60:** 874–906, 1948.

The preservation of the bladder wall surrounding the ureteral orifice has been suggested in an attempt to preserve the so-called "valve action" of the intramural ureter. Either the entire trigone with attached ureters has been transplanted into the sigmoid, or the trigone has been divided and each half transplanted separately.[25–29] These procedures have been mentioned in the literature.[27]

REPORT OF EXPERIMENTAL AND CLINICAL INVESTIGATION

Construction of a tube from a bladder flap. This procedure was done on a total of 16 animals and on 3 patients. All of the tubes remained viable except in two animals; these also had a flap of bladder wall placed around the base of the tube in an effort to form a sphincter; in both, the tube became necrotic and sloughed.

The technique of constructing a tube from a bladder flap which was found to be most satisfactory is as follows:

The bladder is extraperitonealized in all cases which necessitates a flap so long that the dome of the bladder is required in making the flap (fig. 3, *A*). The peritoneum is separated from the bladder except over the area which is firmly adhered to the dome of the bladder. It is incised at this point and the incision is continued around the margin of area of firm attachment, leaving the peritoneum on the bladder over this area. The peritoneum is then closed by approximating its cut edges with 3-0 chromic. Thus the bladder and peritoneum are entirely separated so that a flap taken from the bladder wall can extend entirely over the dome from one side to the other. The flap is made by making an incision through all layers of bladder wall, and another parallel to this is made from 1½ to 4 cm. from it. The flap is left attached to the bladder on one end forming a pedicle a little wider than the flap itself, and the other end is cut off from the bladder. The position of the pedicle varies according to the purpose for which the tube is constructed. The flap is then made into a tube by suturing it around a catheter; the mucosa is on the inside of the tube. Two layers of continuous 5-0 chromic suture are used; the first layer is placed submucous and the second approximates the muscle. The defect in the bladder caused by removing the flap is then closed with two layers of 3-0 chromic—submucous and muscular.

Reconstruction of lower segment of ureter (fig. 1).

Animal research: The lower segment of the ureter was reconstructed with a tube made from a bladder flap in 11 calves. The flap was cut 2 cm. wide and the pedicle left attached to the posterior portion of the bladder in the region of the ureteral orifice. A tube was constructed around a 10F catheter from the flap and its lower end left open into the bladder when the defect in the bladder wall was closed around it. Several methods of anastomosing the upper end of the tube to

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[25] Bergenhem, B.: Ectopia vesicae et adenoma distruens vesicae; exstirpation of beasan; implantation of ureterena i rectum. Eira, 19: 268–273, 1894.

[26] Goodwin, W. E. and Hudson, P. B.: Exstrophy of bladder treated by rectal transplantation of divided trigone; modification of Maydl-Bergenhem operations. Surg., Gynec. & Obst., 93: 331, 1951.

[27] Maydl, K.: Uber die radikaltherapie der blasenktopie. Wien. med. Wchnschr., 44: 25, 1894.

[28] Maydl, K.: Uber die radikaltherapie der ectopia vesical urinariae. Wien. med. Wchnschr., 44: 1113–1115, 1169–1172, 1209–1210, 1256–1258, 1297–1301, 1894.

[29] Mersheiner, W. L., Kolarstick, A. J. and Kammandel, H.: A method for the construction of an artificial urinary bladder by implantation of ureters into completely or partially excluded segments of small intestines. Bull. New York Med. Coll., 13: 71–77, 1950.

the lower end of the severed ureter were used. The one which resulted in the least amount of constriction and fibrosis was an anastomosis of the spatulated ends with 5-0 chromic continuous suture (fig. 1, *A*). This method increases the diameter of the lumen at the site of anastomosis, and prevents a circular ring of fibrosis.

The tube which was reconstructed from the bladder flap remained viable in all eleven calves operated upon. Seven calves died due to faulty technique of constructing a watertight suture line and from difficulty retaining ureteral splints and urethral catheters in these animals. Four calves lived more than one month. In one of these a ureteral stricture developed due to incorrect anastomosis, and one died later from intestinal obstruction due to adhesions. A perfect result was obtained in two calves; no hydronephrosis, infection or other complications occurred. These results show that when proper technique and meticulous care are used, and when it is possible to keep the ureteral splint and a urethral or suprapubic catheter in place for 12 days, a functioning lower segment of the ureter can be reconstructed with a tube from a bladder flap.

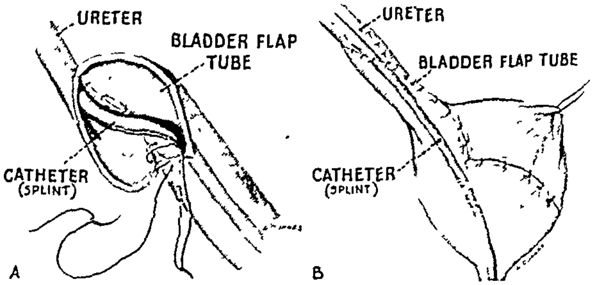

FIG. 1. Reconstruction of lower segment of ureter with a tube from a bladder flap. *A*, direct anastomosis of spatulated end of tube to that of lower end of ureter. *B*, completed reconstruction of lower segment of ureter.

Clinical application: When the lower segment of the ureter is accidentally removed during pelvic surgery, or when excision is indicated for severe stricture, for tumor in a solitary ureter or for other disease, this method of reconstruction can be applied. The authors have done no clinical cases, but Ockerblad,[6] Flocks,[4] and others have reported successful results.

Construction of suprapubic spigot for permanent cystostomy (fig. 2).

Animal research: This procedure was done on 5 animals. A 3 cm. wide flap was cut from the anterior portion of the bladder, leaving a pedicle at the dome (fig. 2, *A*). The tube was constructed around a 18F bag catheter and its lower end left open into the dome of the bladder. The free end of the tube with catheter in place was then brought out through the anterior abdominal wall and skin flaps were brought up on each side to cover the portion of the tube which projects out beyond the abdominal skin surface (fig. 2, *B* and *C*). The catheter was removed in 2 weeks. In order to prevent normal voiding of these animals, the bladder was excised from the urethra at the bladder neck and closed tightly with 3-0 chromic suture in two layers.

This procedure was done on 4 monkeys and 1 calf. In two of these animals, a strip of bladder wall was made to encircle the base of the pedicle in an effort to construct a sphincter at this point; both of these died as a result of necrosis of the tube. One animal died 4 months postoperatively from bilateral hydronephrosis due to contracture of the tube. The two remaining animals lived, but the extra-abdominal projection of the spigot retracted nearly to the level of the abdominal skin; the lumen of the spigot however remained patent and the animals leaked some urine but most of it was passed at intervals corresponding to normal voiding.

Clinical application: Patients who have a permanent suprapubic cystostomy frequently have painful bladder irritation from the suprapubic catheter. If an adequate spigot could be constructed and extend out beyond the abdominal wall far enough to apply a clamp, similar to a Cunningham penis clamp, the patient could remove this to empty the bladder, and a suprapubic catheter would not be necessary. The authors have done this procedure on one patient, but the spigot retracted the same as it did in animals. The construction of a longer tube and longer skin flaps to cover the extra-abdominal portion of the spigot might prevent this retraction.

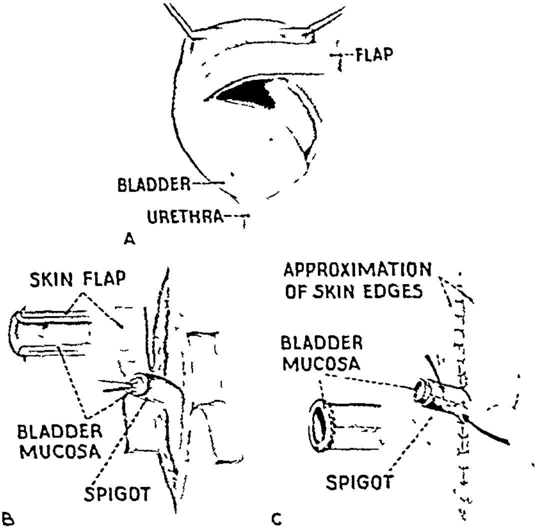

FIG. 2 Construction of suprapubic spigot for permanent cystostomy. *A*, flap cut from bladder wall. *B*, construction of tube from flap and closure of defect in bladder. *C*, completed construction of suprapubic spigot with skin flaps to maintain projection of spigot. Insert shows method of making skin flaps.

Reconstruction of urethra (fig. 3).

Animal research: This was not done in animals because of the technical difficulty of placing a reconstructed urethra under the broad pubic arch and through the small pelvic outlet in these animals.

Clinical application: This procedure can be used to reconstruct the female urethra following its loss by urethrectomy for carcinoma or other disease, or from injury. Other possible applications are its use to construct a urethra in patients with hypospadias, epispadias or exstrophy of the bladder, or in fibrosis of the prostatic and membranous urethra with urinary incontinence.

The authors have done this procedure on two patients and others have reported similar operations with varying degrees of success.

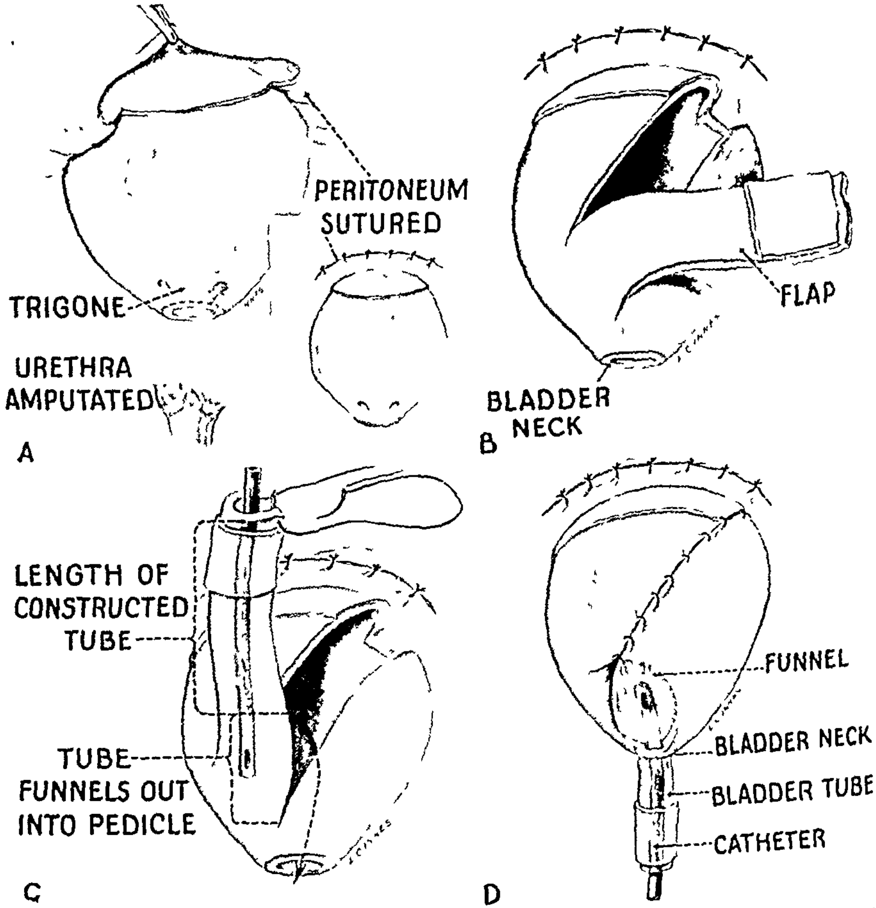

Fig 3. Reconstruction of urethra. *A*, extraperitonealizing bladder to allow procurement of a long flap. *B*, flap cut from bladder wall to reconstruct urethra. Pedicle left near bladder neck on ventral bladder wall. Urethra amputated *C*, tube constructed over 18F catheter Mucosa is on inside of tube. *D*, tube pulled down through bladder neck, bladder neck closed around tube and defect in bladder wall closed.

Technique: The bladder is extraperitonealized (fig. 3, *A*). A flap 3 cm. wide and 14 cm. long is cut from the anterior surface and dome of the bladder, leaving a broad pedicle attached to the anterior bladder wall 3 cm. above the bladder neck (fig. 3, *B*). The tube is constructed around an 18F catheter, beginning the suture at the free end of the flap, and continuing to within 3–4 cm. of its attachment to the bladder wall where the suture line is terminated. The proximal end of the flap is thus left to flare out in a semifunnel shape to the base of the pedicle (fig. 3, *C*). The free end of the tube is then folded downward and pulled out through the bladder neck (fig. 3, *D*), so that the suture line of the tube is at the bladder neck. The bladder wall at its internal orifice is then sutured snugly around the proximal end of the tube, using 3-0 chromic in two continuous layers. A watertight closure is made. The defect in the bladder is then closed. When this procedure follows urethrectomy in the female, the tube constitutes the entire new urethra and extends outward to the vestibule. The undersurface of the tube is covered by vaginal mucosa when there is a sufficient amount of this tissue available; if this cannot be done, the levator ani muscles and other surrounding tissues are brought together beneath the tube to give it support.

Results of clinical application: The urethra was reconstructed following urethrectomy for carcinoma in one female patient. Three weeks following surgery there was normal micturition and only slight leakage of urine which was handled by wearing a pad part of the time. Three years later there was a small mass palpable in the anterior vaginal wall which was suggestive of recurrence.

The procedure was also done to replace a severely fibrosed prostatic and membranous urethra in a man who had complete incontinence following transurethral prostatic resection. The urinary leakage was not controlled although cystoscopy two months postoperatively revealed healthy mucosa lining the prostatic and membranous urethra.

Reinforcing bladder wall and reducing its capacity by overlapping (fig. 4).

Animal research: This was done on one animal in order to determine the ability of over-lapped bladder walls to heal together.

Technique: The bladder is extraperitonealized. A longitudinal midline incision is made through the anterior bladder wall extending from 1 cm. above the bladder neck up over the dome to the upper portion of its posterior wall. On one side the mucosa is denuded from the bladder wall lateralward for 8–12 cm. in the dome (fig. 4, *A*). The denuded area becomes narrower as it approaches both the upper and the lower end of the incision in the bladder, thus forming a fusiform shaped area from which the mucosa has been removed. This side constitutes the upper flap. The other edge of the incised bladder is placed under this flap and sutured to the inner surface of the bladder wall at the lateral edge of the denuded area, using 3-0 chromic continuous (fig. 4, *B*). The lower flap is then overlapped by the upper one and the edge of this outside layer is sutured to the outside of the bladder wall. In this way the entire dome and some of the lateral walls of the bladder are made double thick and the bladder capacity is reduced.

The animal was sacrificed 4 weeks following surgery and the overlapped bladder wall removed and sectioned. It was found to be nearly twice as thick as the wall which had not been overlapped, and histological study revealed complete healing between the two layers (fig. 4, *C* and *D*).

Clinical application: This plastic surgical procedure is indicated in the patient with a large hypotonic bladder which continues to carry much residual urine after all bladder neck and urethral obstruction has been removed. The authors have done it on 2 cases of bladder hypotonia and greatly enlarged bladder capacity resulting from chronic overdistention due to prostatic hypertrophy; removal of the obstructing prostate had reduced the residual urine only a small amount in each case. One patient was entirely relieved of symptoms and residual

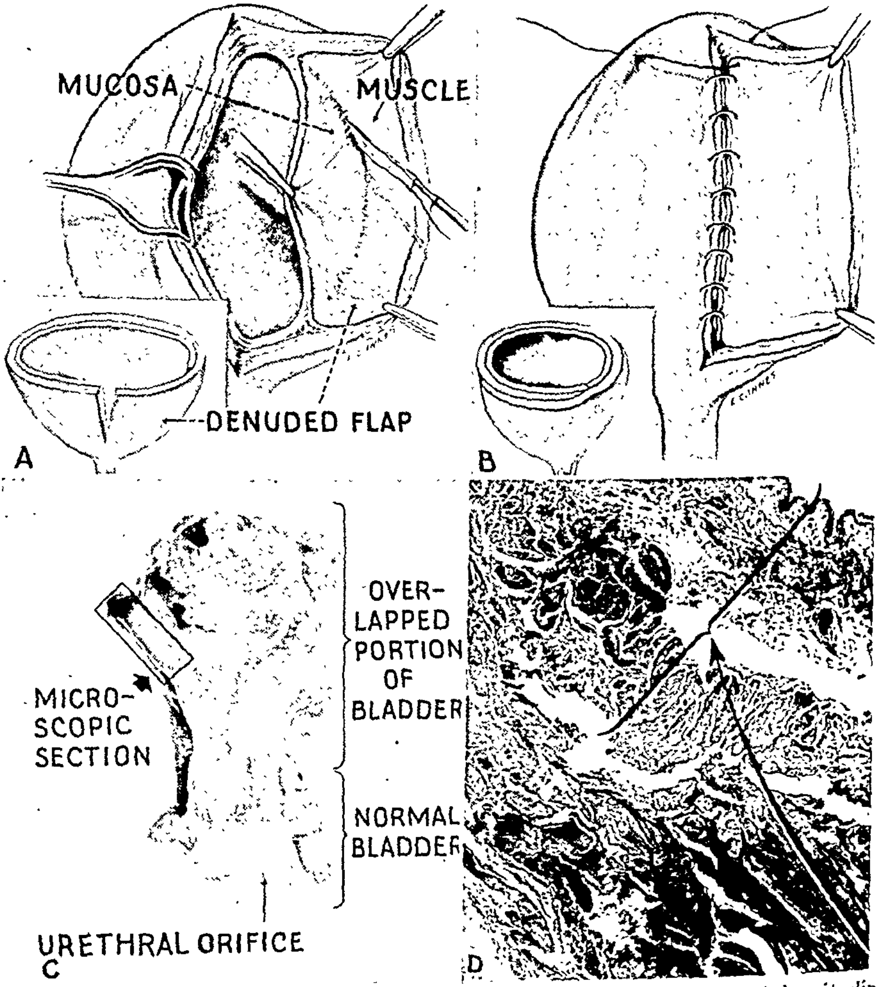

FIG. 4. Re-inforcing bladder wall and reducing its capacity by overlapping. *A*, longitudinal incision in bladder; mucosa denuded from undersurface of upper flap preparatory to overlapping bladder wall. *B*, overlap flaps. Suture edge of inside flap to bladder mucosa first, then suture edge of outside flap to bladder. Insert shows cross section of overlapped bladder wall. *C*, specimen of overlapped bladder wall removed four weeks after surgery. *D*, photomicrograph of cross section of overlapped bladder wall. Note increased thickness of bladder wall. Arrow points to outside layer of overlapped bladder wall.

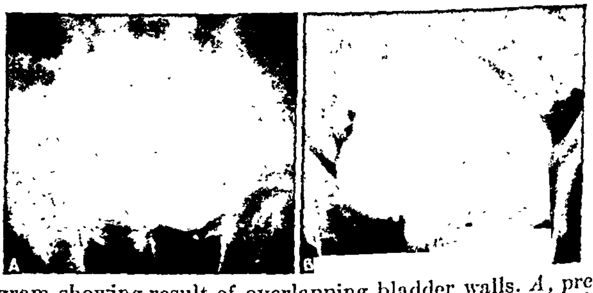

FIG. 5. Cystogram showing result of overlapping bladder walls. *A*, preoperative cystogram made before overlapping bladder walls. Capacity 1500 cc. Residual 400 cc. *B*, postoperative cystogram. Capacity 400 cc. Residual 0.

urine following the overlapping procedure (fig. 5) and the other's residual was reduced three-fourths.

Anastomosis of an isolated loop of intestine to the bladder to increase its capacity (fig. 6).

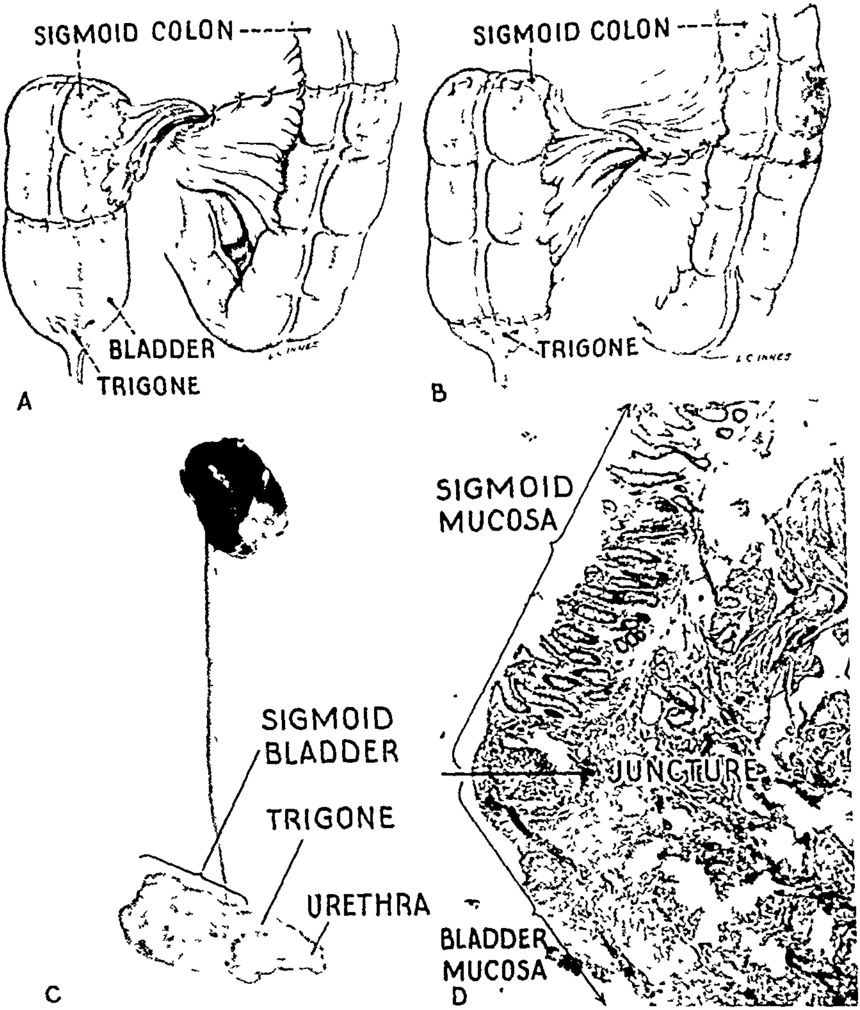

Fig 6 Anastomosis of isolated loop of intestine to bladder to increase its capacity. *A*, isolated loop of sigmoid anastomosed to wide open dome of bladder. End to end anastomosis of sigmoid *B*, entire bladder except trigone excised and isolated loop of sigmoid anastomosed to trigone *C*, photograph of operated specimens to 2 years postoperatively. *D*, photomicrograph of longitudinal section at site of anastomosis.

Animal research: This procedure was done on 7 monkeys. On three the isolated loop of colon was anastomosed to the dome of the bladder; on the other three all of the bladder except the trigone was removed and the isolated loop anastomosed to the trigone. In one additional animal an isolated loop of ileum was used.

Technique: A segment of bowel 10–12 cm. long is isolated by placing intestinal clamps at points which would assure good blood supply to the isolated loop. The segment is excised and the ends of the remaining bowel are re-anastomosed. One end of the segment is closed with a continuous inverting Lembert suture using 5-0 chromic. The dome of the bladder is opened widely (fig. 6, *A*) or all of the bladder wall except the trigone is excised (fig. 6, *B*). The open end of the isolated loop of bowel is then sutured to the cut edge of the bladder wall with a continuous layer of inverting Lembert sutures of 5-0 chromic.

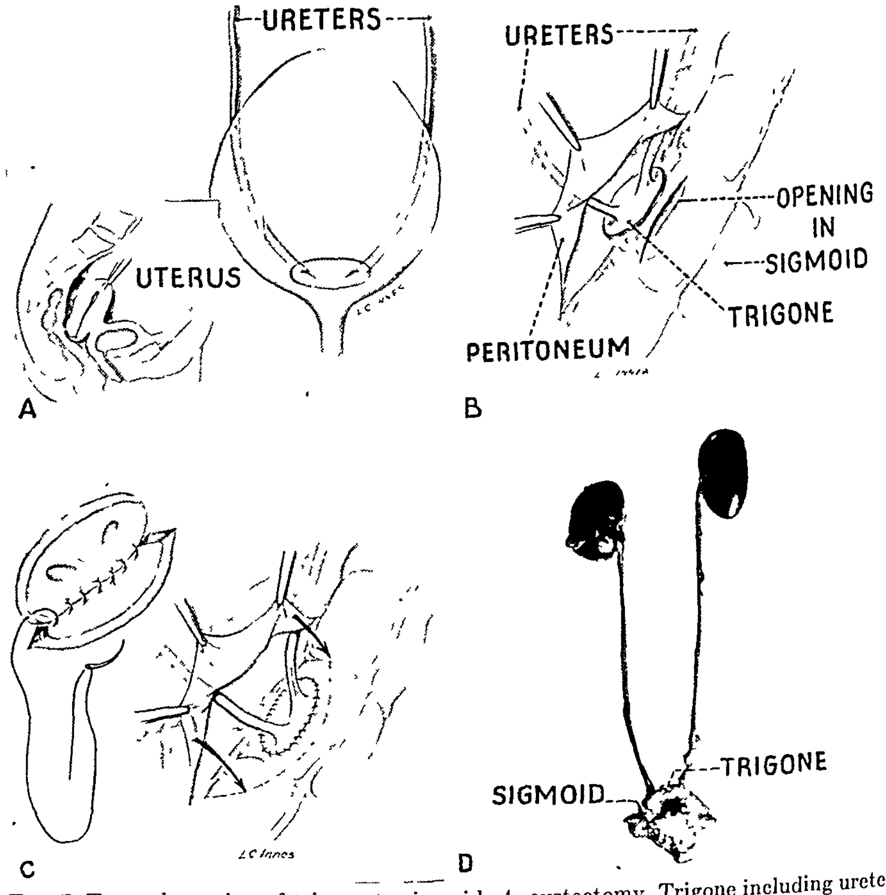

FIG. 7. Transplantation of trigone to sigmoid. *A*, cystectomy Trigone including ureters are preserved. Hysterectomy is necessary when done in female. *B*, trigone and lower end of ureters mobilized. Selection of site for implantation into sigmoid and incision into sigmoid. *C*, trigone anastomosed into opening in sigmoid—mucosa to mucosa suture with 5-0 chromic in two layers. Anastomosis site extraperitonealized. *D*, photograph of anastomosis 3 months postoperatively.

Results of animal research: Of the 6 monkeys which were operated upon, one died of abscess due to leakage through the line of suture and one died of gangrene of the isolated loop of bowel due to poor blood supply. The anastomosed ileum underwent marked dilatation resulting in a dilated atonic bladder. Four animals had an uneventful recovery, the anastomosed colon functioning as a normal bladder (fig. 6, *C* and *D*).

Clinical application: This procedure can be used to enlarge the bladder capacity in cases of interstitial cystitis, excessive fibrosis of the bladder wall and other nonmalignant contracted bladders. The authors have not done it on any patients.

Transplantation of trigone to sigmoid (fig. 7).

Animal research: This procedure was done on 2 monkeys. The bladder was isolated leaving the ureters intact, and all the bladder except trigone with attached ureters was excised (fig. 7, *A*). When done in the female, the uterus was removed in order to obtain adequate mobility of the trigone and lower ends of the ureters. The trigone with the attached ureters were mobilized (fig. 7, *B*) and an incision made in the sigmoid at a point which allowed anastomosis of the trigone without tension on the ureters. The trigone was then anastomosed into the incision in the sigmoid (fig. 7, *C*), using two layers of continuous 5-0 chromic,—one to approximate the muscle layer and a covering serosal line of suture. The area of anastomosis was then extraperitonealized by covering it with posterior peritoneum.

Results of animal research: Both of the monkeys upon which this procedure was done made an uneventful recovery. They were sacrificed three months later and the line of anastomosis between the trigone and the sigmoid was well healed (fig. 7, *D*). There was no dilatation of either ureter or renal pelvis and no evidence of infection.

Clinical application: This procedure may be used in any nonmalignant condition in which it is desired to do a ureterosigmoidostomy. A few of these are: exstrophy of the bladder, incurable vesicovaginal fistula, contracted bladder and urinary incontinence. This study and reports from other authors, most of whom have transplanted each half of the trigone including the ureteral orifice separately, indicate that the results are better by this procedure than when a direct ureterosigmoidostomy is done.

The authors have done no clinical cases.

SUMMARY

Many plastic surgical procedures on the urinary bladder can be done successfully. The profuse anastomosing blood supply, the muscle arrangement of the bladder wall, and the vitality of the mucosa are contributing factors. The results of animal research are reported and the clinical application of the following procedures is discussed:

1) Construction of a tube from a bladder flap
    a. To replace the lower segment of the ureter
    b. To form a suprapubic spigot
    c. To replace or repair the urethra

2) Increasing bladder tone and reducing its capacity by overlapping the bladder walls.

3) Enlarging bladder capacity by anastomosing an isolated loop of sigmoid to the bladder.

4) Bilateral ureterosigmoidostomy by transplanting the trigone into the sigmoid.

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BLADDER TUMOR RECURRENCE IN THE URETHRA: A WARNING

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The purpose of this paper is to call attention to a condition which we believe has not been sufficiently emphasized. This condition is, as the title of the paper states, the recurrence of papillary bladder tumors in the urethra, following primary treatment. Undoubtedly many urologists have seen examples of this type of recurrence but have not attributed any special significance to the fact.

It has long been accepted that implantation of daughter cells can occur from a papillary transitional cell tumor. Albarran, the first modern essayist on bladder and renal tumors, held this view, and it has had many supporters right up to the present time. This apparent seeding can occur on the intact mucous membrane, as is shown where there is spread along the ureter from a tumor of the renal pelvis. Also, tumor implants have often been seen in the scars where open surgery has been done for treatment of bladder tumors. That these occur does not contradict or disprove the hypothesis of the multicentric origin of many multiple bladder tumors, as so ably supported by Kaplan, McDonald and Thompson.

Doctors Reynolds, Schulte and Hammer, in 1948, mentioned the high incidence of "extension into the vesical neck" both initially and after resection. They reported finding of tumor cells in the lymphatics in this area and thought extension to this area was by lymphatic drainage. They acknowledged that the high incidence of bladder neck involvement might be expected in view of the fact that many lesions were late and of the kind usually considered inoperable. It is not these groups to which the present paper refers.

Recurrence in the urethra has probably always occurred in a few scattered cases, but in our experience the incidence seemed to be definitely on the increase. We have seen five instances over the last 6 years, as compared to none in the 10 years preceding. In the first cases, we did not attribute any special significance to the findings. When the next cases appeared, we rather tardily became impressed by the fact and wondered whether it really was occurring more often than before or whether we were looking more closely and merely noticing something that had previously been missed. Inquiry among a few close friends brought variable replies. We then mentioned the condition in the Urological Correspondence Club letter and somewhat to our surprise received a number of replies indicating that others in various parts of the country had noted similar occurrences. We were relieved to find that this was happening to others as well as to ourselves and determined to bring it to the attention of urologists throughout the country at this meeting.

The one main factor in all the cases in which this condition was observed was that the bladder tumor had been treated transurethrally, using the resection instrument, and in four out of 5 cases, transurethral resection of the bladder neck had been done at the same time. It is not unreasonable, particularly in view

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Read at annual meeting, American Urological Association, Atlantic City, N. J., June 26, 1952.

of the individual findings in some cases, to suspect this as an important etiologic factor. These tumor recurrences have appeared usually at the distal edge of the resected area.

The recurrent tumors with one exception, when identified, have been small and not too difficult to deal with. The inherent danger of the condition lies in the possible failure to discover such recurrences in their early stages on routine cystoscopic check-up. If allowed an additional 3 or 6 month period of growth, some of these tumors might begin to infiltrate the prostate and possibly even lead to dissemination before increasing symptoms had forced further diagnostic measures. It is possible that growth of such a tumor recurrence might necessitate radical cystoprostatectomy, whereas early recognition might have allowed simpler treatment. Most serious is the fact that involvement of the prostate has been shown to lead to a higher incidence of generalized dissemination than does infiltration of the bladder wall itself. This has been particularly emphasized by Saphir.

CASE REPORTS

Following are brief abstracts of the cases reported.

C. M., a 68-year old white man, had had dysuria for 4 months. Cystoscopy revealed a large papillary tumor and prostatic hyperplasia. May 1944, suprapubic cystostomy and excision of bladder tumor with coagulation of the base. May 21, 1944, second stage suprapubic prostatectomy. June 30, 1944, cystoscopic examination revealed no evidence of tumor recurrence. May 9, 1946, small papillary tumors, one in the region of the left ureteral orifice and one on the dome of the bladder to the right of the air bubble, were seen. (Prostatic urethra was well healed.) Both tumors were coagulated. February 1948, five small papillary tumors were seen scattered on the left wall. The bladder neck was fibrotic. February 26, transurethral resection of the bladder neck after resection and coagulation of the papillary tumors. Pathological report: papillary carcinoma of the bladder. November 30, 1948, no evidence was seen of tumor in the bladder. Prostatic urethra seemed to have an adequate channel, but just proximal to the external sphincter was a collar of papillary tissue extending around almost the entire circumference of the urethra. December 1948, resection and coagulation of the tumor in the prostatic urethra and coagulation of the areas very close to the sphincter. February 1949, metastases in pubis and ischium.

O. C., a 57-year old white woman, gave a 5 month history of hematuria. Cystoscopic examination showed a papillary tumor 1 cm. in diameter, lateral to the left ureteral orifice. The tumor and base of the stalk were resected, and the base coagulated. Pathological diagnosis: papilloma of the bladder. Cystoscopic re-check in 3 months showed 2 small papillary tumors 4 mm. distal to the vesical neck at 7 and 8 o'clock. The bladder was negative.

F. C. gave a history of transurethral resection of a bladder tumor elsewhere 1 year before our first examination in September 1947, which showed the area of original resection to the left of the vesical neck on the anterolateral wall with a nodular papillary tumor mass recurring in the area and several small papillary tumors of the bladder dome. Suprapubic exposure of the tumors was done with loop resection of the involved areas and coagulation of the base. Pathological diagnosis: bladder carcinoma, malignant type. January 1948, cystoscopic examination showed a reddened area at the site of the original tumor which was resected. A prominent posterior lip was resected. Pathological diagnosis: granulation and fibrous tissue. August 1948, the bladder and bladder neck normal. Just proximal to the verumontanum were two papillary tumor processes, one on each side of the urethra which were coagulated. December 1948, the bladder was normal. A small lesion on the left urethral wall was resected. Pathological diagnosis: bladder tumor. January 1949, all tissues normal except for one small area in the floor of the urethra, which was coagulated. March 1949, 5 mm. area of the right wall of the prostatic urethra resected. Pathological diagnosis: carcinoma. April 1949, no obvious tumor. Three small areas in the urethra, slightly reddened, were resected. Pathological diagnosis: negative. April 1950, no evidence of recurrence.

E. C., a 36-year old white man, gave a history of hematuria for 3 weeks. Cystoscopic examination showed a fairly large papillary tumor whose base could not be seen. April 12, 1948, suprapubic approach revealed a single papillary bladder tumor on a stalk which was severed including the bladder wall surrounding the base. Coagulation of the tumor base was done. Pathological diagnosis: papillary carcinoma, low grade.

June 1948, no evidence of recurrence.

October 1948, no evidence of recurrence.

May 1949, several recurrent bladder tumors on the left lateral wall resected and resection of two bites of posterior vesical lip.

June 1949, several papillary tumors from pinpoint to 1 cm. size on lower left bladder wall with several in the prostatic urethra at the edge of resected area. All tumors were resected or coagulated.

October 1949, no evidence of recurrence.

January and April 1950, no evidence of recurrence.

August 1950, two papillary tumors on the posterior wall coagulated.

October 1950, and February 1951, one papillary tumor coagulated.

July, October and December 1951, no evidence of recurrence.

G. G. a 54-year old white man, had had hematuria 2½ months. Cystoscopic examination showed a papillary bladder tumor 12 mm. in diameter. Transurethral resection of the tumor and base and coagulation of the base were done. A few small bites were taken from the posterior vesical lip. Pathological report: papillary transitional cell carcinoma, grade 2. Six weeks postoperative cystoscopic examination revealed small papillary tumor just distal to the resected area in the prostatic urethra. Bladder negative.

DISCUSSION

Measures which might be taken to prevent this type of lesion would fall into two categories: those directed to prevention of such an occurrence, and those directed to detection of the condition after it has occurred. Naturally, preventative measures deserve first consideration. One way would be to stop doing transurethral resections on bladder tumors. This is, of course, out of the question as the great value of this method of treatment is universally acknowledged.

Another measure would be to destroy the tumor tissue quite completely by the coagulating current at the very outset before resection or other manipulation. We believe that this is an excellent method for small and moderate size tumors. However, it becomes more difficult to follow this plan of attack with larger tumors. It also would be difficult or impossible to carry out in the flat infiltrating type of tumor. All cases which we have seen have been from tumors which were, originally at least, of a papillary nature. Such a method of primary coagulation has the disadvantage of making the resected tumor tissue useless for pathologic studies. This is a serious detriment particularly as regards the determination of infiltration at the base of the tumor.

Certainly the usefulness of irrigation must be considered very carefully. Simple mechanical irrigation should be done with large amounts of solution. Whether solutions of possible cell destroying power such as silver nitrate would be helpful we do not know. One correspondant had already turned to this.

Avoidance of resection of the prostate or bladder neck at the same time that a tumor is treated, we believe, would do most to reduce the incidence of these implants. Our personal feeling is that this is the most important single factor. In several of the cases, the tumor recurrences appeared just at the distal edge of the resected area in the prostate. In one case in a woman, where resection of the bladder neck was not done, we think that the trauma of introduction of the resection instrument was a factor.

Certainly, where preliminary destruction of the tumor by coagulation is not feasible, we think it would be well to avoid resecting the bladder neck or prostate at the same sitting. One correspondant has told us that on the basis of 2 cases in his experience within a year he had abandoned simultaneous resection of tumor and bladder neck. I have done so.

Regardless of the methods used at the time the tumor is destroyed, it is certainly most important to include a meticulous examination of the posterior urethra at each cystoscopic check-up. This can be done well only with the foroblique lens system. The right angle examining lens which is most commonly used for bladder inspections does not allow an adequate inspection of the prostatic urethra. With the concave beak, the posterior urethra cannot be lighted and no inspection at all is possible and even with the convex sheath the view of the urethra is not as good as it should be for such a re-check. We use the McCarthy routine cystoscope using all three telescopes. This allows complete inspection of the entire bladder including the anterior wall and the posterior urethra as well. Only with this instrument (or an equivalent one, such as Young's cystoscope) do we believe that a completely thorough cystoscopic check-up can be done.

SUMMARY

Implantation of papillary bladder tumor cells can occur in the posterior urethra. This seems to follow particularly in cases where transurethral resection of papillary tumors and resection of the bladder neck have been done at the same sitting. We believe that this occurrence is much more common than recognized and that it is increasing in frequency.

The purpose of this paper is to direct the attention of all urologists to the possibility of such an occurrence and urge the adoption of measures to prevent it.

It is important that such tumor recurrence be recognized early before infiltration and possible dissemination occur.

It is suggested that tumor resection and bladder neck resection be avoided at the same sitting.

Other measures which might be applied are thorough irrigation at the time of surgery and possibly the use of cell destroying solutions.

All check-up cystoscopic examinations should include thorough inspection of the posterior urethra.

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END RESULTS IN THE TREATMENT OF BLADDER TUMORS

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Any attempt to arrive at a proper evaluation of the results of treatment of any disease requires not only an extremely careful statistical analysis of cases closely followed but also analysis along the same lines as other investigators so that correlation of end results may be properly made. Flocks[1] has done this admirably in a series of 540 patients all treated 5 years or longer.

I have long been impressed by the general lack of correlation between reports on bladder cancer emanating from different clinics. In many instances it is literally impossible to compare results because of lack of knowledge of what the other author is talking about pathologically.

With this in mind, I have attempted to make this study along the lines of approach suggested by Jewett and Strong[2] and modified slightly by Marshall.[3] I believe that their approach to the problem is not only sound but workable both clinically and pathologically. The relationship of grade of tumor and depth of extension has long been recognized as of prime importance in prognostication.

Jewett[4] has shown that deeply invading tumors of a high degree of malignancy usually are difficult to treat and show poor five year survivals.

Marshall[5] in 104 cases has found that his clinical preoperative estimation as to depth of invasion into the bladder wall was 81 per cent correct. He found that most errors were in underestimating the depth of penetration. This is as I have found it in reviewing our cases.

The author[6] has conclusively proven to his own satisfaction that adequate biopsies properly taken transurethrally will give a true picture of the degree of malignancy of bladder neoplasms.

I should like to add one embellishment to the method described. I now mark the selected piece of tissue for biopsy by transfixing it vertically with a common pin before sending it to the laboratory so that the pathologist may be able to imbed it in the paraffin block in such a way as to make vertical sections (fig. 1). By this method, he can readily see depth of muscle invasion. I have found this to be of great assistance along with the cystoscopic picture and bimanual examination under anesthesia, as described by Jewett. The percentage of error in finding muscle in the microscopic section is practically eliminated.

This study has to do with the results obtained in 386 patients all of whom have been operated upon 5 years or longer.

Three hundred and fourteen or 81.3 per cent have been accurately followed up to the end of the reporting period. Seventy-two cases have been lost, but no

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Read at annual meeting, American Urological Association, Atlantic City, N. J., June 26, 1952.

[1] Flocks, R. H.: J.A.M.A., 145: 295–300, 1951.
[2] Jewett, H. J. and Strong, G. H.: J. Urol., 55: 366, 1947.
[3] Marshall, V. F.: Personal communication.
[4] Jewett, H. J.: J. Urol., 67: 672: 676, 1952.
[5] Marshall, V. F.: J. Urol., 68: 714, 1952.
[6] Milner, W. A.: J. Urol., 61: 917, 1949.

record of their death has been found in the New York State Department of Vital Statistics so for the most part they are presumed to be alive although they are not carried in the report beyond the date of their last examination.

It was interesting to note that cases of papilloma were more difficult to follow than those of cancer. The follow-up on this group was only 58.3 per cent as compared with 86.9 per cent in the cancers.

The more *malignant the cancer the better the follow-up.* In the patients treated by resection and radon seed implantation the follow-up was 90.7 per cent.

All of the records were reviewed and an attempt was made to classify each case as to depth of extension of the tumor. Both the operative description and the pathologic report were of great assistance in most cases. Two hundred and sixty-one cases were so catalogued and it was impossible to classify the remainder.

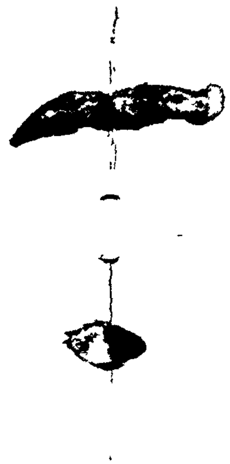

FIG. 1. Pin is placed through biopsy in such a manner as to show deepest and most superficial portions of tumor.

The classification which I will use is that suggested by Marshall as a minor modification of Jewett's original method.

Stage 0 indicates limitation to the mucosa
Stage A: to the submucosa
Stage B_1: to the superficial muscle
Stage B_2: to the deep muscle
Stage C: to the fat
and
Stage D: representing metastases, D_1 being local and D_2 being distant metastases.

Seven cases were not operated upon. They were either moribund or too extensive to make surgery worthwhile.

Suprapubic cystotomy with or without radium or x-ray was used in 27 cases.

Most of these were patients who were treated many years ago before transurethral resection.

Most of these could not be classified as to depth of extension of the tumor. One patient died at the end of 5 years free from tumor and one died of his disease after 8 years. The others died within 24 months, twenty-three dying of their disease within 1 year.

Of those cases of segmental resection (table 1), four have survived 8 years or more without disease, seventeen have died of their disease, eleven during the first 24 months.

TABLE 1. *Twenty-nine cases of segmental resection of the bladder*

YEARS	ALIVE		DEAD		NOT FOLLOWED	
	Without tumor	With tumor	Without tumor	With tumor	Without tumor	With tumor
1			1	6	1	
2			1	5		1
3			1	3		
4					1	
5				1		
6				1		
7						
8	3				1	
9	1					
10						
11						
12						
15				1*	1	
	4		3	17	3	1

Depth of extension; classification: 0, 2; A, 2; B_1, 6; B_2, 8; D_1, 4; D_2, 2; unclassified, 5.
* One lived 15 yrs. with frequent recurrences, treated by transurethral resection.
Operative mortality, 5 cases.

Only seven patients or 24 per cent have survived 5 years or longer. The operative mortality was 5 cases or 17.2 per cent. Several of these cases had subsequent new tumors which were treated by transurethral methods.

Uretero-intestinal anastomosis and cystectomy (table 2) have been done 16 times in this series. All of these patients had serious tumors most of which extended into the deep muscle layer of the bladder or beyond.

One patient or 6 per cent has survived 5 years.

The operative mortality was 3 cases or 18.7 per cent. Eight patients died the first year following operation of cancer and twelve died from their disease by the end of the fourth year.

One patient was operated upon purely for palliation and one required bilateral nephrostomy and colostomy because of complications of surgery.

Cystoscopic fulguration was done in 11 instances. These patients were all old cases treated in the early nineteen thirties. All died of their disease within 24 months. None of the cases could be classified as to depth of extension.

Transurethral resection followed by deep x-ray therapy was used in 7 cases. One case of a papillary, infiltrating, grade 3, type B tumor was negative at the end of 1 year, but the patient has not been seen for check-up since. One case of lymphosarcoma has been negative for tumor for 15 years. This patient was treated by resection, cystotomy and radon and deep therapy.

TABLE 2. *Sixteen cases of uretero-intestinal anastomosis and total cystectomy*

YEARS	ALIVE		DEAD		NOT FOLLOWED	
	Without tumor	With tumor	Without tumor	With tumor	With tumor	Without tumor
1			3	8†, ‡, §		
2				3		
3						
4				1		
5	1*					
6						
7						
8						
9						
10						
11						
12						
	1		3	12		

Depth of extension; classification: B_1, 3; B_2, 6; C, 3; D_1, 4.

* Pt. treated 5 yrs. prior to cystectomy by conservative treatment.

† Operative mortality, 3 cases.

‡ One case operated purely for palliation.

§ One case required bilateral nephrostomy and colostomy.

TABLE 3. *Seventy-two cases of papilloma of the bladder treated by transurethral resection*

YEARS	ALIVE		DEAD		NOT FOLLOWED	
	Without tumor	With tumor	Without tumor	With tumor	Without tumor	With tumor
1			6		15	1
2			4		7	
3			1		2	
4			2		1	
5	6		3		3	
6	5		1		1	
7	5		3			
8	2					
9	2					
10	1					
11						
12	1					
	22		20		29	1

Depth of extension; classification: 0, 46; A, 24, unclassified, 2.

Five patients treated by deep therapy alone were all literally hopeless when first seen and all died in the first 12 months.

Transurethral resection (table 3) was used exclusively for the papillomas of the bladder with the exception of the odd case in which the patient received radiation by radon catheter or x-ray to prevent the multiple recurrences which can be so obnoxious.

Seventy-two patients were treated in this group. Thirty-three of these survived 5 years or longer. Many who were seen when the growth was very small have had recurrences treated by resection or simple fulguration.

Twenty patients have died of other causes.

TABLE 4. *Seventy-six cases of infiltrating cancer treated by transurethral resection and radon*

YEARS	ALIVE		DEAD		NOT FOLLOWED	
	Without tumor	With tumor	Without tumor	With tumor	Without tumor	With tumor
1			5	34	4	1
2			2	5	1	1
3			1	4†		
4			1	2		
5		1	1	2		
6	1		1	1		
7				2‡		
8	1	1	1			
9						
10	1*	1				
11						
12						
13						
	3	3	12	50	5	2

Depth of extension, classification: A, 2; B_1, 25; B_2, 35; C, 5; D_1, 7; unclassified, 2.

* Multiple recurrence of new tumors.

† 1 case of malignant melanoma (secondary).

‡ Sickle cell cancer thought to be due to radiation.

Seventy of these patients were classified as stage 0 or A and two were unclassified. This group adds no significant interest to this paper.

They should practically all be treated by transurethral resection unless the size of the tumor makes this inadvisable for the individual operator.

One of these tumors, a single papilloma on a stalk, 1½ cm. in diameter, weighed 135 gm. Many others weighed from 50 to 100 grams.

Transurethral resection and radon seed implantation (table 4) were done in in 76 cases. Forty-seven of these were classified as B_2 or greater.

Only 2 cases were considered to be in the A group, and two were unclassified.

Fourteen cases or 18.4 per cent have survived 5 years or more. If we consider forty-seven of the 70 patients classified to have had deep tumors, as described by Jewett, with a five year survival expectancy of only 3 per cent, we would anticipate only 1.4 patients would have survived 5 years from this group. This

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1			3	8†, ‡. §		
2				3		
3						
4				1		
5	1*					
6						
7						
8						
9						
10						
11						
12						
	1		3	12		

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	Without tumor	With tumor	Without tumor	With tumor	Without tumor	With tumor
1			6		15	1
2			4		7	
3			1		2	
4			2		1	
5	6		3		3	
6	5		1		1	
7	5		3			
8	2					
9	2					
10	1					
11						
12	1					
	22		20		29	1

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Twenty patients have died of other causes.

TABLE 4. *Seventy-six cases of infiltrating cancer treated by transurethral resection and radon*

YEARS	ALIVE		DEAD		NOT FOLLOWED	
	Without tumor	With tumor	Without tumor	With tumor	Without tumor	With tumor
1			5	34	4	1
2			2	5	1	1
3			1	4†		
4			1	2		
5		1	1	2		
6	1		1	1		
7				2‡		
8	1	1	1			
9						
10	1*	1				
11						
12						
13						
	3	3	12	50	5	2

Depth of extension, classification: A, 2; B_1, 25; B_2, 35; C, 5; D_1, 7; unclassified, 2.

* Multiple recurrence of new tumors.

† 1 case of malignant melanoma (secondary).

‡ Sickle cell cancer thought to be due to radiation.

Seventy of these patients were classified as stage 0 or A and two were unclassified. This group adds no significant interest to this paper.

They should practically all be treated by transurethral resection unless the size of the tumor makes this inadvisable for the individual operator.

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Only 2 cases were considered to be in the A group, and two were unclassified.

Fourteen cases or 18.4 per cent have survived 5 years or more. If we consider forty-seven of the 70 patients classified to have had deep tumors, as described by Jewett, with a five year survival expectancy of only 3 per cent, we would anticipate only 1.4 patients would have survived 5 years from this group. This leaves a total of 12.6 cases surviving 5 years from the group of 27 cases in groups A and B_1, which is nearly a 50 per cent 5 year survival.

Twelve of these patients died from other causes. Five without demonstrable tumor when last seen could not be followed, but no death record could be found in the Bureau of Vital Statistics. This would indicate that 20 cases or 26.3 per cent of the entire group had their disease eradicated as a result of their treatment.

Recurrences of new tumor did occur in some cases and were treated as they appeared.

There were no operative deaths.

TABLE 5. *One hundred forty-one cases of infiltrating cancer treated by transurethral resection alone*

YEARS	ALIVE		DEAD		NOT FOLLOWED	
	Without tumor	With tumor	Without tumor	With tumor	Without tumor	With tumor
1			9	49	18	
2			3	9	8	
3			3	1	1	
4			4	3	4	
5	6		3			
6	4		1			
7	1		3			
8	4*					
9	2*					
10	1*					
11	3*					
12						
13	1					
	22		26	62	31	

Depth of extension; classification: 0, 3; A, 33; B_1, 48; B_2, 34; C, 4; D_1, 18; D_2, 1.

* One case having multiple recurrence of new tumors.

One case adenocarcinoma.

Three cases carcinoma in a diverticulum.

Operative mortality, 2 cases.

Transurethral resection alone (table 5) was used in 141 cases of infiltrating cancer.

Twenty-nine of these patients or 20.6 per cent survived 5 years or more without tumor.

Four cases had multiple recurrences treated as they appeared.

Seventy-nine patients either living or dead remained free from tumor. This represents 56 per cent of the entire group. Again eighteen of these patients were not followed but no record of their demise could be found in the New York State Department of Vital Statistics.

Of course, there was a higher percentage of potentially curable cancers in this group than in those treated by resection and radon. Eighty-four patients of this group fell into the superficial classification, the tumor penetrating the bladder wall no farther than one-half the muscle layer. Of the remaining 57 cases, if we expect a 3 per cent 5-year survival, this would equal 1.7 or roughly 2 cases. That leaves us with 27 cases in the superficial group surviving 5 years or more or a 5-year survival rate of 32 per cent.

Two patients died as a result of their surgery, an operative mortality of 1.4 per cent.

An attempt was made to correlate the survival rates of conservative surgery and that of open surgery (table 6). Unfortunately, the cases of open surgery were too small in number to be statistically significant. Those treated by closed methods are, however, I believe of interest.

TABLE 6

SURVIVAL YEARS	CONSERVATIVE SURGERY; 222 CANCERS GRADED AS TO DEPTH OF EXTENSION												OPEN SURGERY; 39 CANCERS GRADED AS TO DEPTH OF EXTENSION											
	A		B_1		B_2		C		D_1		D_2		A		B_1		B_2		C		D_1		D_2	
	0	X	0	X	0	X	0	X	0	X	0	X	0	X	0	X	0	X	0	X	0	X	0	X
1	9	4	14	17	9	37		8		22				2	1	4	2	4	1	2		8		
2	3		5	3	2	6		2		2						2		2				1		2
3	2		6	4	1	2				1												1		
4	3	1	5	3		3				1						1		2						
5	3		5	3				1							1									
6	3		2			1																		
7	3		1	2	2										1									
8	3		2	2	2										2									
9			1		1																			
10			1		1	1																		
11	1				1																			
12			1																					
13																								
14	1		1																					
15			1			1																		
Total cases	31	5	45	34	20	50	0	11	0	26	0	0	0	2	5	7	2	8	1	2	0	10	0	2

0, without tumor.
X, with tumor.

Here again, I would like to remind you that no papillomas, either with or without atypical cells, were included. All of the cases were definite cancers.

Disease was apparently eradicated by conservative surgery in 31 cases or 86 per cent of the stage A tumors; 45 cases or approximately 57 per cent of the stage B_1 tumors; 20 cases or 28.5 per cent of the stage B_2 tumors; and in none of the stage C or D tumors.

The disease was apparently eradicated by open surgery in none of the stage A tumors; 5 cases or 41.6 per cent of the stage B_1 tumors; 2 cases or 20 per cent of the stage B_2 tumors; 1 case or 33⅓ per cent of the stage C tumors; and none of the stage D_1 or D_2 tumors.

odor. However, the successful repair demands an accurate location of the fistula in relation to the urethral sphincter, trigone, and ureteral orifices. This can be accomplished only by a careful cysto-urethroscopic examination. The defect usually has the appearance of a well-epithelialized opening or as a depressed area with some associated granulation tissue. A small opening may be difficult to see through the cystoscope, but the fistula can usually be demonstrated by filling the bladder with a colored solution and noting the point of discoloration in the vagina. It is often helpful in the accurate localization of the fistulous tract to pass, when possible, a small ureteral catheter from the bladder through the fistulous tract into the vagina. The upper urinary tract should always be checked by an excretory urogram or ureteral catheterization with retrograde pyelogram to rule out any evidence of ureteral trauma, stricture, hydronephrosis, or other organic disease that might alter the program of treatment.

In a patient with a previous diagnosis of carcinoma of the cervix or bladder, a careful search must be made for residual malignant tissue before embarking upon surgical treatment. A detailed history including the cause for the fistula, its duration, and a summary of previous therapy is extremely helpful.

PREOPERATIVE TREATMENT

Adequate preoperative preparation is very important. An untreated infection in the urinary or genital tract greatly increases the incidence of recurrence. Preoperative urinalyses and urine culture with drug-sensitivity studies are essential. Fluids should be forced and appropriate urinary antiseptics and/or antibiotics, depending upon the result of the cultural studies, should be administered. Unless contraindicated the urine should be kept acid. The bladder and vagina should be frequently irrigated with some mild antiseptic solution; for this purpose we have used a 1% sulfathiazole solution. Under no circumstances should the operation be performed until all infection in the bladder or vagina has been eliminated. Some authors have also recommended, as a healing aid, the use of stilbestrol in dosage of 0.5 to 1 mg. daily in women past the age of menopause.

SURGICAL CLOSURE OF FISTULA

No one surgical approach is applicable in all cases. The surgeon after reviewing the diagnostic findings should use that approach, either vaginal, transvesical, transabdominal, or any combination of these, that he believes will give him the best exposure and the greatest likelihood of a cure. Generally speaking we believe that a fistula whose vesical opening is near the bladder neck or in the trigone can be best handled by the vaginal approach, whereas a fistula posterior to the trigone, especially if associated with scaring and fixation of the anterior vaginal wall, can be more easily closed transvesically. In the vaginal approach we have found that placing the patient on her abdomen with legs spread apart and with elevation of her buttocks by breaking the table or raising the kidney elevator gives a better exposure than the lithotomy position. In the suprapubic approach the incision in the abdominal wall and the bladder, whether longitudinal or transverse, should be sufficiently long to make the fistulous opening easily accessible.

After the fistula has been clearly exposed the mucus lining and scar tissue from the rim of the fistulous tract should be removed by sharp dissection (fig. 1). If the opening is near a ureteral orifice, the ureter should be catheterized before surgical closure is begun, and the catheter should be left in place during the operation so as to minimize the danger of injuring the ureter. Next, the wall of the bladder should be separated from that of the vagina for a distance sufficient to permit the approximation of the bladder wall without tension. All bleeding must be controlled since excessive bleeding may jeopardize the ultimate outcome.

The vaginal and bladder walls are then closed separately. The one to be sutured first will depend upon the surgical approach. We believe that the most important step in the surgical repair of the fistula is the accurate and complete closure of the vesical wall without tension and with inversion of the vesical mucosa. This requires accurate and precise placement of the sutures. The direction or configuration of the suture line is of no importance so long as the above criteria have been met. Probably no one suture material justifies its sole use to the exclusion of others. We believe that catgut on an atraumatic needle is as good as any and have used it routinely, with gratifying results.

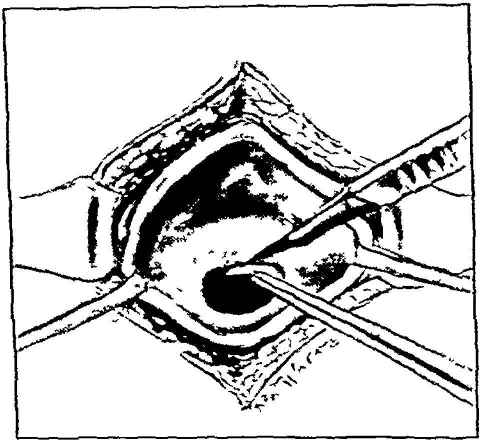

FIG 1. Excision of scar tissue and mucus lining from rim of fistulous tract in transvesical approach.

In the vaginal approach the bladder wall is of necessity closed first by interrupted sutures of No. 1 atraumatic chromic catgut, carefully placed so as to include the entire bladder wall except the mucosa so that when tied the bladder mucosa is inverted (fig. 2). Just enough sutures are used to accurately and snugly approximate the bladder wall without strangulation of the blood supply. This row of sutures is fortified by a second one of interrupted sutures of the same material. The vaginal wall is likewise closed in two layers: the first, a layer of interrupted No. 1 atraumatic catgut mattress sutures placed sufficiently far back from the margins of the wound to draw the vaginal wall up against the bladder wall; the second, a layer of interrupted atraumatic catgut sutures to close the vaginal mucosa. The vagina is lightly packed with plain gauze. A 24F dePezzer catheter is inserted through the urethra.

In the suprapubic procedure, the vaginal wall is first closed with one or two layers of interrupted No. 1 atraumatic chromic catgut sutures depending upon its relaxation. The bladder wall is accurately approximated by the same type of suture material, a vertical type of mattress suture being used. The deep limb of this suture goes through the entire thickness of the bladder wall, placed about 5 mm. behind the wound margin. The anterior limb merely picks up the bladder mucosa and the superficial layers of the bladder wall at the edge of the bladder incision. These sutures are tied just tight enough to firmly approximate the opposing edges of the bladder wall without tension (fig. 3). If, after the above sutures have been tied, there is any gaping of the margins of the mucus membrane, additional simple interrupted No. 00 atraumatic catgut sutures are inserted to issure a perfect union. The suprapubic wound is closed about a 24 or 26F dePezzer catheter brought out at the upper angle of the incision.

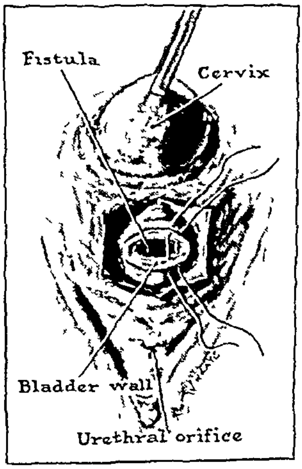

FIG. 2. Placement of sutures for closure of the vesical wall in vaginal approach.

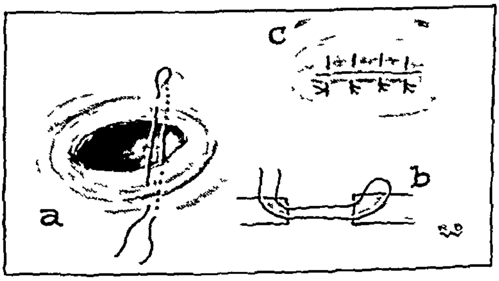

FIG. 3. Placement of sutures for the closure of vesical wall in transvesical approach *a*, Suprapubic view *b*, Side view. *c*, Sutures tied

POSTOPERATIVE CARE

The care of the patient during the immediate postoperative period rates next in importance to the actual closure of the defect. A constantly maintained collapsed bladder is absolutely imperative for prompt healing after any method of repair. A single overdistention of the bladder may produce a failure in an otherwise perfectly executed program of treatment. The importance of a freely draining catheter should be explained to the patient. The patient along with the nurses, intern, and resident must keep a constant watch to see that the drainage tube does not become blocked or kinked. The catheter should be irrigated frequently, especially while the urine is bloody, with small amounts of saline solution. The catheter should be connected to a bottle tied at the side of the bed, and under no circumstances should it be clamped or plugged. The urethral catheter should be changed every 6 to 8 days to lessen the likelihood of calcareous deposits.

In an effort to keep the incision for the closure of the fistula dry, postural drainage is used. The patient is placed in a prone position for six to eight days postoperatively. When suprapubic catheter drainage is used, the patient is placed either on a Bradford frame or on a split mattress so that the drainage tube can be run from the patient directly to the floor so as to prevent kinking of the drainage tube. With an indwelling urethral catheter the connecting drainage tube is run down between the patient's legs to the foot of the bed, thus making it unnecessary for the tube to go either over or under one of the patient's legs. Some authors object to this position because it becomes extremely uncomfortable and they believe it may actually be harmful. Miller believes that the prolonged prone position may predispose to embolism. It is true that the patient becomes uncomfortable in this position, but a little extra nursing care in the form of minor adjustments in the patient's position, replacing of pillows, gentle massage, and vocal encouragement keeps her cheerful and happy. In our small series we have not had any complications attributed to the position of the patient.

The suprapubic catheter is replaced by an indwelling urethral catheter as soon as the patient is removed from the prone position. Indwelling catheter drainage is kept up for a minimum of sixteen to twenty days. Postoperatively the patient is given methylene blue, gr. 1, b.i.d. at intermittent intervals to facilitate the detection of any urinary drainage from the operative site. After removal of the catheter the patient is asked to void at least every 2 hours, is checked at the end of 8 hours for residual urine, and is watched closely for any evidence of vaginal drainage. If any urinary vaginal drainage is detected the patient is immediately put back on continuous indwelling catheter drainage for another 5 to 7 days. We believe that some of the failures in this type of surgery can be attributed to an insufficient period of postoperative catheter drainage.

Postoperatively the patients are given a house diet, encouraged to force fluids, and are given acidifying reagents to keep the urine definitely on the acid side. The preoperative urinary antiseptics and/or antibiotics are continued as long as the indwelling catheter is in place or until the urine becomes entirely negative. The vaginal pack is removed at the end of 48 hours.

We have successfully treated six consecutive cases of long-standing vesicovaginal fistula by following the program just outlined. We believe these cases are worthy of mention.

CASE REPORTS

Case 1. A 30-year-old woman was admitted to the hospital in March 1943, with the history that she had had incontinence of urine for 13 years. She insisted that the leakage of urine started following an appendectomy. She wore a perineal pad constantly. For the preceding 6 months she had had intermittent attacks of gross hematuria associated with some discomfort in the suprapubic area. She had a left nephrectomy 8 years previously in another hospital.

On physical examination grossly bloody urine was trickling from the vaginal outlet. Pelvic examination was normal except for considerable redness of the vaginal mucosa and a small fistulous tract in the midanterior vaginal wall from which urine was oozing. Cystoscopic examination disclosed a small fistula in the midtrigone just inside the bladder neck. There was an associated generalized encrusted alkaline ulcerative cystitis. The urine showed considerable pus with E. coli organisms on culture. The excretory urogram showed a normal right kidney and right ureter. The left renal shadow was absent.

The patient was treated for 1 week preoperatively with indwelling urethral catheter drainage, bladder irrigations with an acid solution, vaginal douches, and ammonium chloride and urotropin as a urinary tract antiseptic.

The fistula was closed by the vaginal approach with the patient in the lithotomy position. A 4F ureteral catheter was passed through the fistulous tract immediately before the operation. The fistulous tract was excised. The vaginal and bladder walls were separated for a distance of one cm. The bladder wall was closed by interrupted atraumatic catgut sutures, with inversion of the mucosa. Postoperatively the patient was placed in the prone position for 5 days and on continuous indwelling catheter drainage for 15 days. She was given sulfadiazine, gm. 1, q. 6 hours for 4 days postoperatively, then changed over to ammonium chloride and urotropin. At no time postoperatively was there any vaginal urinary drainage. Following the removal of the catheter she voided freely.

The patient was last seen in the out-patient department in January 1949, at which time she was pregnant. There were no urinary symptoms. The patient had no vaginal drainage. The urine was entirely negative. The patient had a normal pregnancy with cesarean section about two weeks before the expected date. There were no untoward reactions from the pregnancy.

Case 2. A patient was admitted to the hospital in October 1943, with the history that she had had complete incontinence of urine for the preceding 5 years. This started several days following the birth of her first child. Apparently she had a large baby with a difficult delivery. Since that time she had had 4 operations for repair of the fistula, all done by the vaginal approach, and each one was unsuccessful. One year previously, she had another baby born by cesarean section. The patient was very depressed because she was unable to keep herself dry and clean. The perineal pad which she was forced to wear, along with the dribbling of urine, kept up a constant irritation of the skin about the genitalia.

On cystoscopic examination the patient was found to have an opening about 1 cm. in diameter situated in the midportion of the trigone just beyond the internal urethral orifice leading to a fistulous tract which ran down within the vesical vaginal septum and emptied into the vagina just in front of the cervix, slightly to the left of the midline. A ureteral catheter could readily be passed through the fistula, which was left in place until the time of the operation. The upper urinary tract was normal on intravenous urogram. Urinalysis was negative. A urine culture was sterile.

The patient was treated preoperatively for 2 days with sulfadiazine, gm. 1, q. 6 hours, and bladder irrigations and vaginal douches twice daily using a 1 per cent sulfathiazole solution. The operation was carried out by the vaginal approach with the patient in the prone jackknife position. The fistulous tract was excised. The bladder and vaginal walls were separated for a distance of 1½ cm., and the former was closed by interrupted atraumatic catgut sutures with inversion of the vesical mucosa. Postoperatively the patient was placed in the prone position for 5 days. She had continuous indwelling catheter drainage for 16 days. At no time was there any noticeable urinary vaginal drainage. She was kept on sulfadiazine for 3 days postoperatively then changed over to ammonium chloride and urotropin. At the time of discharge on the eighteenth postoperative day she was voiding freely with good control.

She was last seen in the out-patient department 8 months postoperatively, at which time she was symptom free and had a good bladder capacity. There was no residual urine. The urine was clear and microscopically negative.

Her recent reply to a follow-up letter stated that she had remained well, and had no further leakage of urine.

Case 3. A 63-year-old woman was admitted to the hospital in January 1948, with the history that she had had incontinence of urine for 10 years. This began several days after a total hysterectomy. Since that time she had had four unsuccessful attempts to close this fistula, all by the vaginal route. Up until two months before admission she was able to control the leakage of urine fairly well by wearing a pessary, but since then she had been totally incontinent.

On physical examintion there was urine flowing from the vagina. There was a large fistulous opening in the anterior superior portion of the vaginal vault, with hyperemia of the vaginal mucosa.

On cystoscopic examination there were noted two fistulous openings in the posterior wall, each about 1 cm. in diameter, separated by a small bridge of bladder mucosa. A ureteral catheter could be readily passed through the fistula into the vagina. Urinalysis was negative. A urine culture was sterile. Intravenous urogram revealed a normal upper urinary tract.

The patient was treated preoperatively for 2 days by forcing fluids, sulfadiazine, gm. 1, four times daily, and bladder and vaginal irrigations with a 1 per cent sulfathiazole solution.

Surgical repair was carried out by the transvesical approach. The mucosa and scar tissue about the margin of the fistulous tract were excised, making one large fistula. The bladder wall was separated from the vaginal wall for a distance of 1 cm., and the former was closed by interrupted vertical mattress sutures, with inversion and careful approximation of the vesical mucosa. The suprapubic wound was closed about a dePezzer catheter.

Postoperatively the patient was kept in the prone position for 8 days. The suprapubic catheter was removed on the eighth day, and an indwelling urethral catheter inserted. The patient was kept on constant catheter drainage until the twentieth postoperative day. At no time was there any vaginal drainage. The patient was given penicillin and sulfadiazine for 4 days postoperatively then changed over to mandelamine, 750 mg., four times daily. Following the removal of the catheter she voided freely with good control.

She was seen in the out-patient department in May 1948, at which time she was symptom free and had no vaginal discharge. She was voiding in large amounts. The urine was negative. A recent communication informed us that she has remained entirely symptom free.

Case 4. A 20-year-old patient was admitted to the hospital in May 1949. She was delivered of an eight-pound baby in January 1949, following which she developed leakage of urine through the vagina. This had continued until the time of admission despite several attempts by the vaginal route to close the fistula. The patient would void occasionally in small amounts, but most of the urine drained through the vagina.

On physical examination there was urine trickling from the vaginal outlet. Several wire sutures could be palpated in the anterior vaginal wall. On cystoscopic examination there was seen just beyond the internal urethral orifice in the midtrigone area a depressed area in the center of which was a small fistulous opening. This opening was surrounded by an area of granulation tissue, and the ends of several wire sutures could be seen protruding through the vesical mucosa in the immediate vicinity of the vesical opening. A 4F ureteral catheter could be fed easily through the fistula and entered the vagina in the midanterior vaginal wall. The urine was negative. A urine culture was sterile and an excretory urogram showed a normal upper urinary tract.

The patient was treated for 48 hours preoperatively by a free fluid intake, vesical and vaginal irrigations, and penicillin and dihydrostreptomycin given intramuscularly. The fistula was closed by the vaginal approach with the patient in the jackknife position. Eight wire sutures were removed, some of which were deeply imbedded in the tissues about the fistulous tract. The margin of the fistulous tract was excised by sharp dissection, and the bladder and vaginal walls were separated for a distance of one-half cm. The vesical opening was closed by atraumatic catgut sutures with invagination of bladder mucosa. A 24F dePezzer catheter was inserted through the urethra.

Postoperatively the patient was placed in the prone position for 5 days. She was kept on constant indwelling urethral catheter drainage for 14 days. The dihydrostreptomycin and penicillin were continued for 6 days postoperatively. At no time during this period did she have any drainage of urine from the vagina. Following the removal of the catheter she voided freely with excellent control.

She was last seen in September 1949, at which time she was symptom free. There was no vaginal drainage. The urine was clear and microscopically normal. The bladder capacity was 400 cc and there was no residual urine. The patient has moved to another part of the country and could not be followed.

Case 5. A 51-year-old woman was admitted to the hospital in April 1950, with the history that for the past 25 years, since the birth of her last child, she has had constant leakage of urine through the vagina, with the passage of only small amounts of urine through the urethra. She complained of considerable vaginal and labial irritation. There had been no previous attempts at surgical repair. In February 1950, she had a severe attack of left renal colic, following which she passed a small irregular urinary calculus.

On physical examination there was considerable redness and irritation of the skin about the external genitalia and of the vaginal mucosa. Urine was trickling from the vagina. The cervix was somewhat reddened and granular with a laceration extending laterally into the right fornix. This laceration seemed to be completely healed except for a small opening near its lateral margin from which was trickling some watery fluid.

Cystoscopic examination showed a well epithelialized fistulous opening about ½ cm. in diameter in the posterior wall just above the interureteric ridge. Otherwise the bladder appeared normal. A bilateral retrograde pyelogram showed a normal upper urinary tract. Urinalysis was negative except for 20 white blood cells per high power field. A urine culture produced E. coli.

The patient was treated several days preoperatively with a free fluid intake, mandelamine therapy, and irrigations of the bladder and vagina with a 1 per cent sulfathiazole solution.

The fistula was closed by the transvesical approach. It was found to be about 5 mm. in diameter, situated just above the trigone to the right of the midline. Clear urine was spurting from each ureteral orifice. A 5F ureteral catheter was passed up the right ureter and was left in place during the course of the operation. The fistulous tract was excised about 2 mm. beyond the margin of the fistula. The bladder was separated from the vagina for a distance of at least a cm. and the opening in the bladder was closed by interrupted vertical mattress sutures. The suprapubic incision was closed about a 26F dePezzer catheter.

Postoperatively the patient was placed in the prone position for 9 days. On the ninth day the suprapubic catheter was removed and an indwelling urethral catheter was inserted. At no time postoperatively was there any evidence of vaginal urinary drainage. The patient was given duracillin, 400,000 units, and streptomycin, 0.5 gm., intramuscularly twice daily for the first 4 postoperative days. Mandelamine was continued during the entire postoperative period. After removal of the catheter the patient voided freely with good control and without any vaginal drainage.

She was last seen in the out-patient department in June 1950, at which time she was symptom free. The urine was clear and microscopically negative. A reply in answer to a follow-up letter stated that she has remained entirely well.

Case 6. This 40-year-old woman was admitted to the hospital July 8, 1951, with the chief complaint of "a hole in my bladder and no control of my urine." She gave a history that in December 1936, she was treated with radium and x-ray for carcinoma of the cervix. Following this she was well for 4 months, then became constipated and apparently developed a rectovaginal fistula. She went untreated for 5 years, during which time there was fecal drainage through the vagina. In 1941, an intestinal obstruction apparently developed, and was treated by a permanent colostomy. The patient was then well until August 1950, when she noticed pain in the right lower quadrant associated with marked frequency and urgency of urination; within a few days she developed total incontinence of urine. During the year prior to her admission she had numerous cystoscopies, and apparently on several occasions had fulguration of the fistulous opening without any improvement in her symptoms.

At the time of her initial examination she was completely incontinent unless wearing a small mushroom catheter, which would decrease the drainage about 50 per cent. On pelvic examination there was urine trickling from a markedly contracted scarred vagina. Because of the fixation of the tissues the fistulous opening in the vagina could not be visualized. On digital examination the opening could be readily felt high up on the anterior vaginal wall, and the index finger could be inserted through the fistula into the bladder.

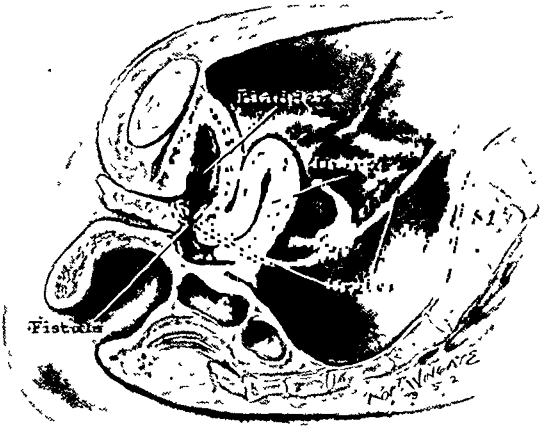

FIG. 4. Sagittal view showing ureterovesicovaginal fistula.

Cystoscopic examination was unsatisfactory because the bladder could not be distended. However, it was evident that there was a large fistulous opening about 2 cm. in diameter on the floor of the bladder just posterior to the trigone. This portion of the bladder seemed to be retracted and fixed. Both ureteral orifices were seen and appeared normal. Urinalysis showed a few pus cells with E. coli on culture.

A scout film showed no shadows of any urological significance. An excretory urogram revealed prompt function with good concentration of dye by both kidneys. The internal architecture of the left upper urinary tract appeared normal. On the right there were slight hydronephrotic changes in the renal pelvis and some dilatation of the pelvic portion of the ureter. On the 60-minute film there was a moderate amount of retention of dye on the right side.

Surgical closure was attempted by the suprapubic approach. A large fistulous opening 2 cm. in diameter was found in the base of the bladder just posterior to the right side of the trigone. The fistula was well epithelialized. It was found that there was a complete break in the continuity of the right ureter, and that its proximal stump emptied into the fistula (fig. 4). It was believed that the defect could not be satisfactorily closed without first eliminating the urinary drainage from the right kidney. No attempt was made to close the fistula at this time.

A right nephrectomy was done several days later. The diagnosis was chronic pyelonephritis and hydronephrosis of the right kidney.

The patient had an uneventful convalescence from these two operations. Twelve days after the nephrectomy the lower abdominal incision was reopened and the fistula was closed transvesically. The margin of the fistulous tract was excised and the vaginal wall was separated from the vesical wall for a distance of a cm. or so. In doing this, the peritoneum was inadvertently opened but was immediately closed. The defect in the bladder was closed without tension by a row of atraumatic vertical mattress catgut sutures and a superficial layer of atraumatic fine catgut sutures. The suprapubic wound was closed about a 26F dePezzer catheter.

Postoperatively the patient was placed in the prone position for 10 days. On the tenth day the suprapubic catheter was removed, and an indwelling urethral catheter was inserted. She was kept on continuous indwelling catheter drainage for 3 weeks. Following the removal of the catheter there was slight intermittent drainage of urine from the vagina. Cystoscopic examination at this time showed that the site of the closure of the fistula was well healed except for one very small opening at the medial margin. The opening was about 1 mm. in diameter and seemed to be in the process of healing. A urethral catheter was re-inserted and she was again kept on continuous indwelling urethral catheter drainage for an additional three weeks. Postoperatively she was continued on mandelamine and terramycin. The latter drug was kept up for a total of 6 days. After removal of the urethral catheter on the forty-fifth postoperative day the patient voided normally except for some urgency. There was no vaginal urinary drainage.

She was last seen on February 8, 1952, at which time she was voiding freely, with good control of her urine. She said she was able to hold as much as 400 cc urine in her bladder at a time. The urine was clear and microscopically normal. There was no residual urine. The patient is back at work and is extremely happy with the results.

SUMMARY

A well established vesicovaginal fistula usually requires surgical treatment. No one method of approach or operation is applicable to all fistulas. Accurate diagnosis and adequate preoperative preparation, especially the control of any genitourinary infection, are important preoperative requisites.

In the surgical closure the approach is optional, providing adequate exposure is obtained. It is imperative, however, that the defect, especially in the bladder wall, be meticulously closed without tension and with inversion of the vesical untreated for 5 years, during which time there was fecal drainage through the vagina. In 1941, an intestinal obstruction apparently developed, and was treated by a permanent colostomy. The patient was then well until August 1950, when she noticed pain in the right lower quadrant associated with marked frequency and urgency of urination; within a few days she developed total incontinence of urine. During the year prior to her admission she had numerous cystoscopies, and apparently on several occasions had fulguration of the fistulous opening without any improvement in her symptoms.

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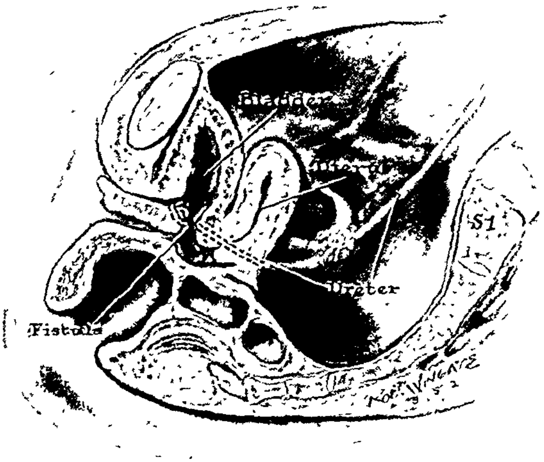

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In the surgical closure the approach is optional, providing adequate exposure is obtained. It is imperative, however, that the defect, especially in the bladder wall, be meticulously closed without tension and with inversion of the vesical mucosa after first removing the epithelialized surface and scar tissue from the fistulous tract.

Continuous, unobstructed, catheter drainage with the maintenance of a completely collapsed bladder must be carried out postoperatively until healing is complete. This usually takes from 14 to 21 days. Appropriate chemotherapy and/or antibiotics should be used as indicated for control of any genitourinary infection.

Six consecutive cases of vesicovaginal fistula, successfully treated by surgical closure, are reported.

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RECONSTRUCTION OF THE PERINEAL URETHRA WITH A FREE FULL-THICKNESS SKIN GRAFT FROM THE PREPUCE

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The clinical picture of so-called chronic urinary extravasation, although diminishing in recent years, is still seen on the wards of large charity hospitals and remains a challenging problem to the urologist. This condition consists essentially of a chronically indurated peri-urethral phlegmon usually associated with multiple abscesses and urethral fistulas to the perineum and scrotum, the "sprinkle-pot" perineum of the older urological literature. The penis, scrotum and perineum become markedly enlarged due to the brawny induration, persistent low-grade cellulitis and lymphangitis, so that the term elephantiasis has been properly applied.

Most of these patients have a history of recurrent urethritis with the subsequent formation of a urethral stricture. Periodic urethral dilatation is performed at variable intervals and following any one of these manipulations peri-urethritis may occur due to the trauma inflicted in the presence of a chronically infected urethral stricture. This may develop into a localized peri-urethral abscess or a spreading cellulitis or phlegmon. In acute cases, multiple incisions of the infected areas must be performed together with a cystotomy or perineal urethrotomy in order to relieve the associated urinary retention and to place the urethra at rest. The sequelae of such repeated peri-urethral infections is the formation of multiple urinary fistulas extending from the urethra to the skin of the scrotum and perineum. In many of these patients there also develops one or more chronic walled-off deep-seated abscesses from which sinuses form to the skin and drain purulent material intermittently. The end result is a thickened, indurated perineum and scrotum containing draining sinuses and multiple urinary fistulas. In the more severe cases the anterior urethra becomes a mass of dense scar tissue which is impermeable to the smallest filiform so that the patient voids entirely through the multiple perineal fistulas.

The surgical approach to chronic peri-urethral phlegmon is based upon two factors. First, diversion of the urinary stream is accomplished by a cystotomy to allow for subsidence of any acute infection in the peri-urethral tissues. Secondly, excision of all chronically infected tissue in the perineum and scrotum is performed. An attempt is then made to reconstruct the perineal urethra so that patency of the urethra is re-established. Reconstruction of the urethra in most cases is accomplished by excision of the scarred portion and the insertion of an indwelling urethral catheter for a long period of time. Experience has shown that epitheliazation will occur across the urethral defect with the indwelling urethral catheter acting as a splint. However, the newly formed urethra

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will usually recontract and reform a stricture so that periodic dilatation must be continued and recurrent peri-urethritis may develop.

Several methods of reconstruction of the excised portion of the scarred urethra have been described in recent years in an attempt to prevent reformation of the stricture. Most of these reports have dealt with impassable urethral strictures secondary to the trauma of war wounds. By means of a dermatome or special skin-grafting knives, a split-thickness graft is obtained from other areas of the body such as the arms, thighs or abdomen. The free graft is used to bridge the urethral defect by wrapping it around an indwelling catheter and suturing it to each end of the exposed urethra. This technique is reported to yield a high percentage of takes with a good anatomical and functional result.

In order to simplify this method and obviate the use of a dermatome or special skin-grafting knives we have modified the technique using a free full-thickness skin graft from the prepuce.

CASE REPORT

J. C., a Negro, aged 50, was admitted to the Cook County Hospital July 6, 1950, with a 10-year history of an enlarged, recurrently painful scrotum. For the past few years he urinated completely through several openings in the scrotum. He had an old history of several episodes of gonorrheal urethritis, 20 to 25 years ago, following which a urethral stricture developed and required periodic dilatation. On several occasions during the past 10 years he had acute painful swelling of the scrotum after being dilated. These swellings were incised and pus was evacuated each time. On one occasion 7 years ago he was hospitalized and a perineal urethrotomy was performed. He has noted intermittent drainage of pus from the scrotum and for the last few years all voided urine has passed through several openings in the scrotum and perineum. There were no other pertinent facts in the previous history.

Physical examination was essentially negative except for the local findings A brawny induration of the perineum and scrotum was present and also several small fistulous openings in the lower portion of the scrotum some of which drained pus. The patient voided voluntarily and had complete control but all the urine passed through several of these fistulous openings in the scrotum. Rectal examination was negative.

He was treated with antibiotics and hot, wet compresses to the perineum and scrotum. A suprapubic cystotomy was then performed. Three weeks following this he was discharged from the hospital and told to return to the clinic for follow-up care. During the next few months some of the induration in the perineum and scrotum subsided and there was only slight drainage of pus from the fistulous openings. He was readmitted to the hospital at this time for definitive surgery.

On November 15, 1950, surgery was performed under spinal anesthesia with the patient in the lithotomy position. All of the thickened, indurated portions of the scrotum and the perineum containing the fistulous tracts were excised down to the perineal urethra. A sound could be passed as far as the perineal urethra where it met with an impassable stricture. This was seen to consist of a cord of dense scar tissue for a distance of about 1½ inches. This portion of the urethra was completely excised. The two ends of the urethra above and below the stricture were seen to be patent and relatively normal in appearance. A 24F sound could be passed without difficulty into the bladder from the proximal cut end of the urethra and through the entire length of the penile urethra from the distal cut end. A 20F straight catheter was passed from the urethral meatus, through the penile urethra, across the excised portion of the urethra, through the proximal portion of the urethra and then into the bladder. An ordinary circumcision was then performed and a cuff of prepuce was removed from the penis about ¾ inch in width and 2 inches in length. This was wrapped lengthwise around the exposed portion of the catheter in the perineum with the skin surface facing inwards toward the catheter. The redundant portion of the graft was trimmed and it was sutured lengthwise together with interrupted sutures of 0000 chromic catgut. Each end of the graft was then sutured to the adjacent ends of the normal urethra with similar type catgut (fig. 1). Two small Penrose drains were inserted in the perineum and the skin was closed with fine silk.

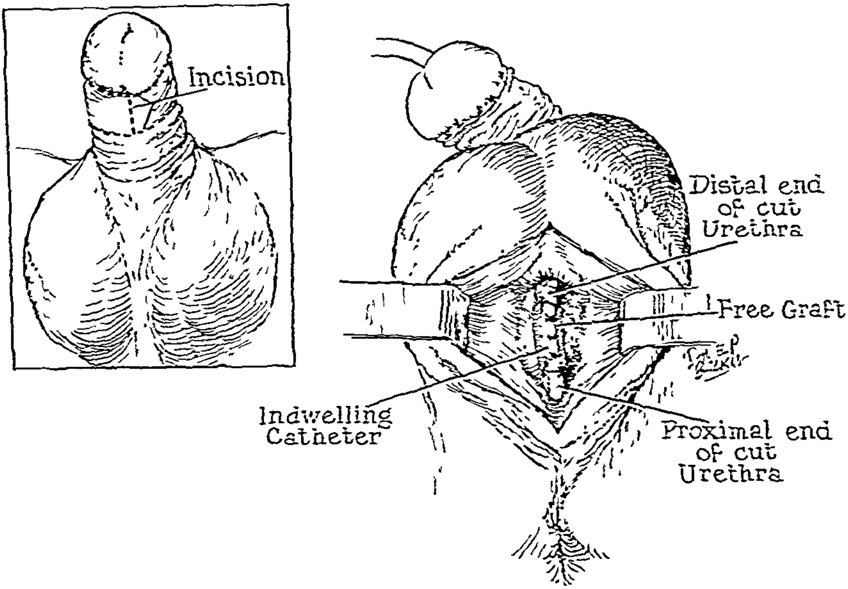

FIG. 1. Diagrammatic representation showing line of incision for removal of prepuce and position of prepuce skin graft around catheter in perineal urethra

The patient had an uneventful postoperative course and the wound healed primarily. There was no evidence of slough of the graft. The urethral catheter and cystotomy tube drained freely. The urethral catheter was removed after 2 weeks. Four weeks postoperatively a 20F sound was passed through the entire length of the urethra without difficulty. Several days later the cystotomy tube was removed. One week later the cystotomy wound was healed and dry and the patient voided normally with a good stream from the urethra.

The patient has been seen several times since surgery but has refused further dilatation or catheterization. He is voiding without difficulty and has no urinary complaints.

CONCLUSIONS

A simple technique utilizing the skin of the prepuce as a full-thickness graft for reconstruction of the excised portion of an impassable urethral stricture has been described. The successful result in one case has been very encouraging and its further trial is warranted in order to establish the true value of this procedure.

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INFILTRATION OF THE PROSTATE GLAND BY CHRONIC LYMPHATIC LEUKEMIA

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While chronic lymphatic leukemia commonly involves the kidney,[1] the prostate as a site of involvement has been reported only 4 times.[2, 3, 4, 5] Because of its apparent rarity we wish to report two more cases of leukemic infiltration of the prostate. Some degree of benign prostatic hyperplasia co-existed with the infiltration in each case.

CASE REPORTS

Case 1. M. B. L., a white man, aged 62, was admitted to La Crosse Lutheran Hospital November 4, 1947, complaining of inability to void during the past 18 hours. He had been well and active up to 2 days prior to admission. At this time he noticed that his urinary stream was becoming slower and slower until it finally stopped entirely. During the past several years he had noted increasing frequency and nocturia. Eight years previously he had required catheterization on one occasion.

System inquiry revealed no tendency toward weakness or bleeding.

Physical examination showed a well-developed man. Blood pressure was 165/80. The chest was clear; the heart seemed normal. In both axillae could be felt enlarged nodes. These were discrete, nontender and of moderate size. The spleen was barely palpable below the costal margin. The bladder was palpable below the umbilicus as a soft, round mass. Rectal examination showed the prostate to be very large (4 plus), but soft, symmetrical and smooth.

The patient was catheterized and 500 cc dark, but clear urine drawn off. Medical consultation was obtained.

Upon admission the nonprotein nitrogen was 26 mg per cent; hemoglobin 11.4 gm.; red blood cells 4,100,000; white blood cells 150,000 with lymphocytes 94 per cent, neutrophils 5 per cent, eosinophilic myelocytes 0.5 per cent, stem cells 0.5 per cent. The platelet count as well as the bleeding and clotting times were within normal limits. The urine was negative except for a few red and white blood cells microscopically. X-rays of the chest and kidneys, ureters and bladder were negative.

Two days after admission a transurethral resection was performed. The resectoscope sheath was held much tighter than usual by bulging intra-urethral

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[2] Jacobi, M., Panoff, C. E. and Herzlich, J.: J. Urol., 38: 494–499, 1937.

[3] McCrea, L. E.: Urol. & Cutan. Rev., 44: 694–695, 1940.

[4] Hare, D. M., Spence, H. M. and Fuqua, F.: J. Urol., 62: 845–848, 1949.

[5] Connor, J. J., Heinemann, S. and Macnish, J. M.: Urol. & Cutan. Rev., 54: 276–279, 1950.

masses in the prostatic area. This made manipulation of the instrument slightly difficult, but no other problem was encountered. No excessive bleeding was noted and no postoperative irrigation of the catheter was required. The highest postoperative temperature was 100.5F on the day of operation and also on the following day. In 48 hours the catheter was removed and the patient then voided with ease.

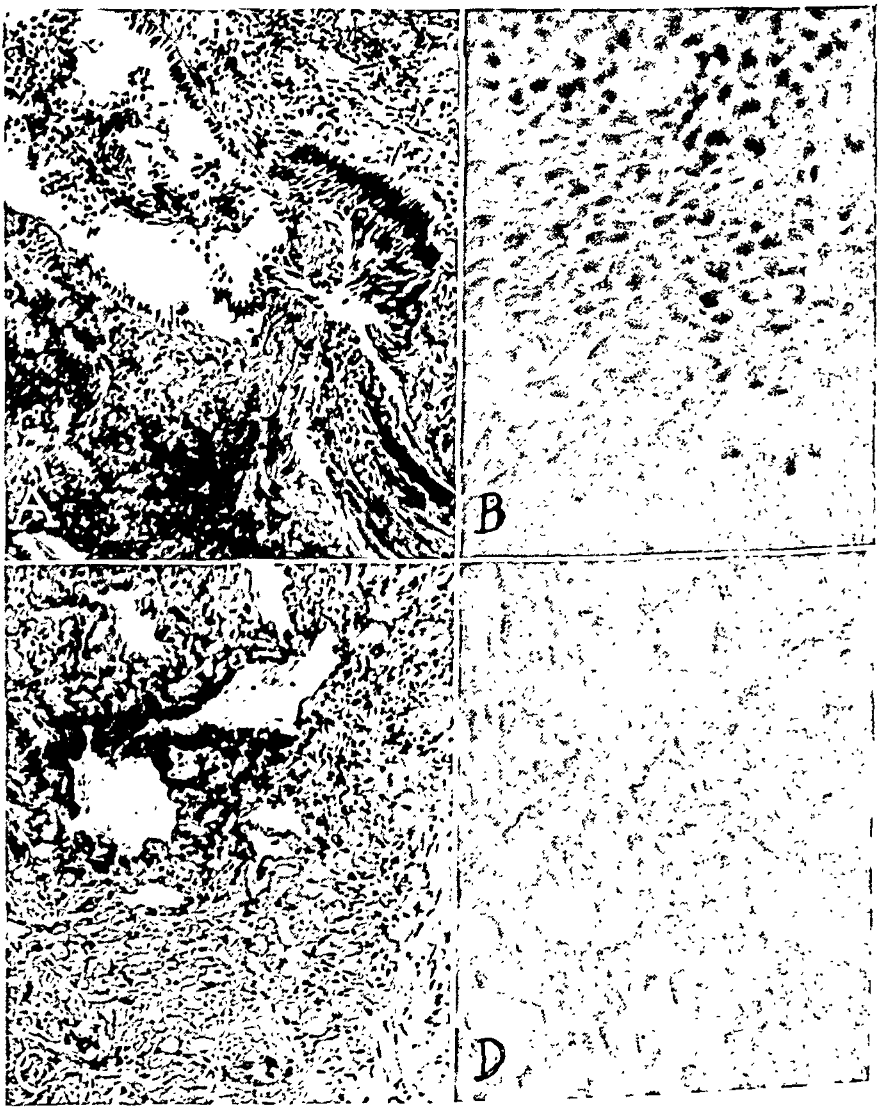

FIG. 1

Pathology report (by Dr. M. Sivertson): Diagnosis, leukemic infiltration of the prostate; benign prostatic hyperplasia. The gross specimen weighed 69 gm. Microscopic examination of sections from the prostate revealed an enormous amount of cellular infiltration. These occurred in massive areas and also in layers between the smooth muscle tissue and were seen everywhere in the sections. These cells were apparently of the lymphocytic series with hyperchromatic nuclei and gave the appearance of leukemic infiltration. A moderate degree of benign hyperplasia was also present (fig. 1, *A* and *B*).

Five days following the transurethral resection, 150 r was administered to the splenic area. The white blood cell count at this time was 90,000. The patient was then allowed to go home, to return 2 weeks later. He did not appear at this time, nor subsequently. However, he is known to have gotten along well and was in good health until sometime in the Spring of 1950, when he died of pneumonia.

Case 2. E. L. O., a white man, aged 76, was admitted to St. John's Hospital December 27, 1949, complaining of generalized aching, occasional vomiting and urinary frequency during the previous 3 weeks. Although he had been getting up at night to urinate 2 times for a number of years, he recently had noted increasing nocturia up to 5 times. Some slowing, dribbling and difficulty in starting the stream were also noticed. Recently he had lost 12 pounds in weight.

Physical examination showed a slender, aged, underweight individual who was chronically ill. The blood pressure was 130/80. The heart was not enlarged; no murmurs were present. The chest was clear. The spleen was enlarged one finger below the costal margin. Questionable enlargement of the liver was present. By rectal examination the prostate was enlarged 2 plus, smooth, symmetrical and soft.

Laboratory studies showed the white blood cell count to be 200,000 with 98 per cent lymphocytes (table 1).

X ray of the chest was interpreted as follows: "The tenth rib in the posterior axillary line showed an area of rarefaction which may be an artefact; however, the seventh rib anteriorly shows a mottling with thinning of the cortex and a periostitis indicative of destruction and repair. This is compatible with leukemic involvement."

Three treatments of 125 r, 100 r and 100 r were given over the spleen together with daily anterior and posterior body spray radiation to a total of 100 r during a one-month preoperative period. During this time a urinary tract infection (Pseudomonas aeruginosa) was treated with catheter drainage and antibiotics. The red blood count had risen from 2.61 million to 3.78 million with the aid of blood transfusions and the general condition had improved. It was hoped that the patient might make a recovery without surgery, but a trial without a catheter was unsuccessful. He was therefore given further blood transfusions and prepared for surgery.

On January 25, 1950, a transurethral resection of the prostate together with a bilateral vasectomy was performed. Introduction of the 28F sheath was easy. Intra-urethral lateral lobes, grade 2, with intravesicular enlargement, grade 1, were seen. Resection was carried out without difficulty and no unusual bleeding was encountered.

Pathology report (by Dr. E. Palik): Diagnosis, lymphocytic infiltration of the prostate, compatible with lymphatic leukemia; benign glandular hyperplasia of

TABLE 1. *Case 2. Laboratory studies*

DATE	12-21-49	12-28-49	12-31-49	1-3-50	1-9-50	1-16-50	1-21-50	1-24-50	1-25-50	1-26-50	1-31-50	3-17-50
Rbc	3.29 Ml	2.61	3.29	3.13	3.32	3.97	3.87	3.78	Transurethral prostatic resection and bilateral vasectomy.	3.99	3.17	2.0
Hb (grams)	9.2	7.0	9.1	10.1	9.6	9 9	8.8	11.3		10.8	12.0	8 3
Wbc	216,000	200,000	75,700	65,000	78,500	48,000	33,000	35,000		31,000	19,000	6000
Neutrophil	0	1	5	5	4	11	12	18		27	21	9
Myelocyte	0	0	0	0	0	0	0	0		0	0	0
Juvenile	0	0	0	0	0	0	0	0		0	0	0
Band	0	1	1	2	0	7	5	4		4	3	3
Segmented	4	0	4	3	4	4	7	14		23	18	6
Lymphocyte	96	98	95	93	95	87	88	82		73	79	91
Mononuclear	0	0	0	0	0	2	0	0		0	0	0
Eosinophil	0	1	0	1	0	0	0	0		0	0	0
Basophil	0	0	0	1	1	0	0	0		0	0	0
Platelets	72,820	x	x	144,000	146,000	108,000	130,000	120,000		88,000	80,000	x
Bleeding time	6 min.	x	x	x	x	x	x	1½ min.		x	x	x
Coagulation (Lee-White)	7 min.	x	x	x	x	x	x	6 min.		x	x	x
Prothrombin	x	x	x	75.5%	x	x	x	86.5%		x	x	x
NPN	54 (mgm.%)	42										
Kline	neg.	x	neg.	x	x	x	x	x		x	x	x
Blood trans. 500 cc.	x	yes	x	yes	yes	x	yes	yes	yes	x	x	x

the prostate. The gross specimen consisted of pink and tan ribbons of tissue measuring up to 2 cm. in length, and weighing 30 gm. Microscopic examination of the tissue showed that the glands throughout the prostate presented moderate epithelial hyperplasia. The interstitial tissues of the prostate in many areas were infiltrated by dense collections of lymphocytes (fig. 1, *C* and *D*).

The patient's immediate postoperative course was surprisingly uneventful in view of his previous difficulties and frail constitution. The highest postoperative temperature was 100.5F, registered the day of surgery. The catheter required no irrigation and was removed in 48 hours. He then voided well and on the sixth postoperative day was discharged home. The white blood cell count on discharge was 9,000.

The patient continued to do well, although the urinary tract infection continued for 3 months. At this time the urine became clear and remained so. During the Fall of 1950 he was again hospitalized for treatment of an acute lobar pneumonia.

DISCUSSION

Case 1 illustrates a case of lymphatic leukemia of considerable chronicity. For this reason the onset is difficult to determine. It would seem that the patient had increasing difficulty from benign hypertrophy for about 8 years. This difficulty was then augmented by the development of leukemic infiltration in the prostate. He was treated by transurethral resection without regard to his leukemia. Aside from the slight increase in difficulty in moving the resectoscope sheath about, nothing unusual from that seen in an ordinary benign case was noted.

Case 2 represents a more rapid onset of leukemia, with more systemic symptoms and a rapid increase of urinary symptoms. Since it has been suggested that radiation of the prostatic area is the treatment of choice in this condition,[2] it was hoped that the patient might have received enough scatter radiation to adequately shrink the prostate. However, this did not occur and transurethral resection again was performed without difficulty, or with any indication that the gland was other than benign. Increased tendency to bleeding has been mentioned as a problem in these cases;[5] this was not noted in either of our cases.

SUMMARY

Two cases are added to the literature of infiltration of the prostate gland by chronic lymphatic leukemia, to the 4 already reported. These cases were associated with benign prostatic glandular hyperplasia.

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OSTEITIS PUBIS TREATED BY CORTISONE

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Osteitis pubis has become a major complication of prostatic surgery occurring from weeks to months following the patient's apparent recovery from his initial surgery. It is a painful, disabling inflammation of the pubes, ischii and at times the spine. It tends to involve all the elements, cartilage, periosteum, bone and the attaching ligaments. The onset may be insidious or fulminating. The acute stage is stormy and incapacitating, and the convalescence may be long delayed. It is believed that most of the cases follow suprapubic operation on the bladder but according to reports other operative procedures may cause osteitis pubis, and, in occasional instances, nonoperative conditions such as pyelonephritis, septic abortion, and normal delivery.

Beer, in 1924, first described the syndrome and gave a description of most of the facts as they are recognized today. There are many reported cases of osteitis pubis in the literature but we believe the actual instances far outnumber them.

It is not the intention of this paper to deal with the various theories advanced as to the causative factor in the disease nor to attempt to differentiate between osteitis, osteomyelitis, and atrophoneurosis. Hock and Kurtz in their excellent article reviewed the previous concepts of the disease and attempted to explain osteitis on the basis of a causalgic process originating from an inflammatory process within the pelvis. Lavalle and Hamm explain osteitis as a subacute inflammatory infiltration and chronic inflammation involving the periosteum, bone and cartilage. They explain osteitis as a bacterial infiltration of low virulence and pathogenicity. We believe a pre-existing urinary infection is usually present even though it appears to be controlled by the use of antibiotics. Whatever the direct causative factor may be, we are all agreed on the symptom complex which makes osteitis such a problem: the time element of its appearance, the distinctive pain over the pubic bone, extension to the thighs, marked adductor spasm of one or both legs, and partial or complete immobilization of the patient. The x-ray appearance of the pelvic girdle usually confirms the diagnosis. While the disease is self-limited and spontaneous healing occurs, the patient may be incapacitated for from several weeks to months or a year.

Treatment of these cases with antibiotics on an infectious basis has been generally unsatisfactory. From a review of cases treated these patients have run the gamut of therapy: antibiotics; narcotics, with the possibility of addiction; diathermy; injections of antibiotics; injection of novocaine in the prostatic capsule; incision and drainage; casts and immobilization; use of anticoagulants; deep x-ray therapy and many others. None of these measures have been specific for all cases. Recently, Marshall et al. have reported 3 cases of osteitis pubis treated with ACTH with dramatic results. Considering that osteitis pubis is an

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inflammatory disease involving bone and adjacent structures, the thought occurred to us that the manifestations might be benefited by the use of cortisone just as it is in diseases such as rheumatoid arthritis, acute rheumatic fever, fibrositis, etc. The response was prompt and almost miraculous. Pain disappeared in from 24 to 48 hours, patients were out of bed, and walking on the third day. Pressure pain over the pubes and adductor muscles disappeared and the patients were relieved and comfortable. The remarkable part of the treatment is that recurrence has not occurred. We would like to present three cases of osteitis pubis treated with cortisone from the Urological Department of the Wilkes-Barre General Hospital.

CASE REPORTS

Case 1. T. S. (B-55375) aged 60, was admitted to the Wilkes-Barre General Hospital August 7, 1950, with acute urinary retention. This was associated with a history of urinary difficulty for approximately 6 months prior to admission. He had nocturia 3 times, poor stream, and some terminal dribbling. The physical examination was essentially negative except a bladder distended half way to the umbilicus that was tender on pressure, and a grade 3 enlargement of the prostate. The gland was smooth, slightly tender on pressure, nonnodular, and could be mobilized. There was no evidence of cancer. Catheterization recovered 850 cc clear urine. The catheter was left in for drainage. Cystoscopy revealed a homogeneous enlargement of the gland with absence of tumor or stone. There was marked bladder trabeculation. X-rays of kidneys, spine, pelvis and bladder were normal. The impression was benign prostatic hyperplasia and prostatectomy was recommended.

Laboratory studies: Blood urea nitrogen, 11.8 mg. per cent; sugar, 92 mg. per cent; hemoglobin, 12 gm.; red blood cells, 3,800,000; white blood cells, 8,200, with normal differential. Urinalysis: albumin, trace; sugar, negative; 50 to 60 white blood cells per high power field.

A suprapubic prostatectomy was done August 10, 1950, with a routine prophylactic bilateral vaso-section and ligation. The closure was routine with a No. 24 urethral Foley, and a No. 26 Robinson suprapubically and a small drain in the prevesical space. The drain was removed in 24 hours, the suprapubic catheter in 48 hours, and drainage from the urethral catheter was uncomplicated. Seven days postoperative the patient had a delayed hemorrhage which necessitated evacuation of clots through the resectoscope. The bladder was evacuated, hemorrhage was controlled and drainage was re-established. The catheter was removed on the ninth day and the patient voided. However, he was very apprehensive and the catheter was re-inserted. It was removed on the thirteenth day, the patient voided well, and was comfortable. He was discharged on the sixteenth day, August 26, 1950, as improved.

The pathological report on the gland, which weighed 85 gm., was nodular hyperplasia without malignancy.

The patient was re-admitted September 18, 1950. Approximately 7–10 days following discharge from the hospital following prostatectomy, the patient complained of pain in the lower back, thighs bilaterally, and extending down the legs. The onset was gradual but then would become very intense and then subside. The pain increased with attacks of pain over the pubic bone, down each thigh and out to the legs, lasting 6 to 8 hours and requiring a narcotic for relief. X-ray examination showed osteoporesis of both descending rami of both pubic bones with roughening and thickening.

He was treated with antibiotics, narcotics, and hot dressings to the pubis.

He was discharged September 20, 1950, as unimproved.

The patient was re-admitted October 11, 1950. He complained of severe pain over the pubic bones extending down the thighs producing definite difficulty in walking. The blood studies showed a normal CBC and blood chemistry. Urine examination showed a slight trace of albumin and 8–10 pus cells per high power field.

Manual examination produced pain over the pubic bones with pain on pressure over the adductor muscles. Difficulty was experienced in moving the legs due to intense pain.

He was treated with narcotics for pain and subjected to a course of deep x-ray therapy.

He was discharged October 21, 1950 as unimproved.

The patient was treated at home with sedatives, narcotics, massage, heat therapy, etc., for 4 weeks. He suffered a great deal of pain and was unable to walk. He lived between his bed and a couch. He became very despondent, lost his appetite, and began to lose weight. On a sudden inspiration he was treated with cortisone. The dosage was started November 1, 1950, with 100 mg. hypodermically every 8 hours for the first day. This was reduced to 100 mg. every 12 hours for the next day, and then continued at 50 mg. twice a day for 1 week. The pain was relieved somewhat the first day. He was able to walk the second day, and on the third day he was able to walk out of the house. At the end of a week he had no pain or distress, and pressure over the pubes and the thighs caused no discomfort. The cortisone was then continued 50 mg. daily for 2 weeks. This man has been under observation at regular intervals since that time and has had no recurrence of any of his previous symptoms. X-ray examination of the pelvis reveals increased calcification with some roughening of the pubes and new bone formation. The urine was microscopically clear.

Case 2. H. B. (B-61926) aged 81 was admitted by ambulance to the Wilkes-Barre General Hospital on June 13, 1951. The provisional diagnosis was osteitis pubis with urinary incontinence. The patient was a feeble old man who had had a retropubic prostatectomy elsewhere three months previously. The operation, according to the history, was a difficult procedure complicated by hemorrhage. He made an uneventful recovery with the exception of a total incontinence and left the hospital wearing a Cunningham clamp. Three weeks before admission to the General Hospital, he began to have increasingly severe pain suprapubically and this was followed by excruciating pain in the right leg and groin. He was unable to move and was bedridden. His physical examination showed a blood pressure of 175/100 with a fair myocardium. A freshly healed suprapubic scar was present. Rectal examination showed a thickened prostatic capsule and some palpable tissue. The patient wore an incontinence clamp. Extreme pain was present over the pubis and along the right thigh, and was intense on pressure over the course of the obturator nerve. The patient was unable or unwilling to move the leg or to move in bed.

Urine studies showed a trace of albumin, no sugar, and a few white blood cells. Blood studies: hemoglobin, 65 per cent; red blood cells, 3.25; white blood cells, 12,200, with normal differential. Blood urea nitrogen, 12.5 mg.; blood sugar, 91 mg.

X-ray examination of the pelvis and spine showed cortical thickening with increased porosity of both pubis bones and ischii.

X-rays were typical of osteitis pubis.

Cortisone 300 mg. given 100 mg. by hypodermic every 8 hours for 24 hours. The next day the patient was able to move in bed with less distress. The drug was reduced to 100 mg. every 12 hours. June 16, 1951, the patient was out of bed, sitting in chair and able to move legs with very little pain. Pressure over the thigh and pubis caused no distress. Marked improvement in sense of well being was noted. Cortisone reduced to 50 mg. every 12 hours. June 17, pain had almost entirely disappeared and the patient was able to walk in the room and around the hall without distress. June 19, marked improvement was noted. The patient was sleeping well and moving in bed freely. He complained of only a very slight amount of pain on pressure over the pubis and thigh. The cortisone was continued, 100 mg. By June 21, the over-all picture had improved. There was a noticeable amount of euphoria. The patient felt better, ate much better, was walking, and had no distress. He was discharged, to continue cortisone 100 mg. daily for one week.

The patient has been under regular observation since his discharge from the hospital. There has been no recurrence of the osteitis pubis syndrome. X-rays showed that the condition in the pubic bones was still present, but with increased density and no extension of the process.

Case 3. V. A. (B-61023) aged 65 ,was admitted to the urological service of the Wilkes-Barre General Hospital on April 30, 1951. He had complete retention and was relieved by catheterization and then indwelling catheter. He had previously had some retention and had been catheterized on several occasions. Following the last attack he was admitted to the hospital for evaluation and treatment. The physical examination showed a nervous patient with a hypertension of 210/120, and a fairly good myocardium. The abdomen was distended suprapubically with an overfull bladder. Rectal examination revealed a smooth, symmetrical gland enlarged to a grade 2 plus, and with no evidence of cancer on palpation.

Laboratory studies: Hemoglobin, 13 gm.; red blood cells, 4.03; white blood cells, 12,000, with normal differential. Blood urea nitrogen, 17.3 mg.; blood sugar 88 mg.

An excretory urogram showed normal kidneys with bladder normal in contour and size. The shadow of an enlarged prostate was present. No shadows of calculi were seen. The bone structure was normal. No evidence of metastasis was detected.

Eight days after admission, when the patient had become quiet and all tests were made, a one stage suprapubic prostatectomy was performed. The operation was uneventful. A urethral and a small suprapubic catheter were inserted and a drain in the prevesical space. The drain was removed in 24 hours, and the abdominal catheter in 48 hours. Patient was ambulatory in 24 hours. The urethral catheter and all sutures were removed on the seventh day. Patient voided well and had no distress. He walked around the ward and recuperated until the twelfth day when he was discharged. His condition was excellent. He voided well, there was no residual and only occasional smarting at the end of urination.

The diagnosis was nodular hyperplasia with inflammation. The gross specimen weighed 68 gm., and revealed no evidence of carcinoma.

The follow-up was satisfactory. The urine became free of infection. Micturition was satisfactory; he had nocturia once. Six weeks following prostatectomy, the patient presented himself at my office with the aid of a companion and a cane. He complained of intense pain suprapubically and in his right thigh and leg. The pain was gradual in onset and then in the last few days had become very intense. Examination of the urine showed only an occasional white blood cell, and no albumin.

X-ray examination showed an increased density and increased porosity of both pubes. The ischii were not involved. There was no malignant infiltration. The diagnosis was osteitis pubis.

This patient was immediately put on cortisone therapy with the usual dose of 300 mg. the first day; 200 mg. the second day, and than a maintenance dose of 100 mg. daily. This dosage was all given orally, and the relief was nil. He returned after one week of trial therapy worse instead of better. He was then instructed to maintain a daily dose of 300 mg. of cortisone until there was improvement in his symptoms before reducing the dose. However, the next day his son, a priest, came to the office with a very illuminating story. The second bottle of tablets did not look like the first bottle. The second bottle was purchased through a hospital pharmacy and the reason for the change was that he had heard that the first pharmacist was not considered entirely reliable. With the cortisone obtained from the hospital, and in less than 24 hours, the patient showed a marked improvement and the dosage was reduced as per the original plan. His pain had disappeared in 3 days and the patient was able to walk without a cane and minus the pain. He continued the cortisone for a period of 2 weeks and then stopped. He has been under observation for the past 10 months and has had no recurrence of the symptoms of osteitis pubis.

X-ray examination showed regression of the porosity and increased calcification and thickening of the cortex.

DISCUSSION

Of all the distressing complications of prostatic surgery, osteitis pubis is one of the worst. The patients are incapacitated, dehabilitated and in extreme pain, topped off with a profound mental depression associated with suicidal tendencies. In spite of our knowledge that the condition is self-limited, this reassurance to the patient is not very helpful. The previously mentioned methods of treatment, at least in our hands, have been fruitless. Anyone who has had such a disheartening complication will appreciate our grasping for a new form of therapy.

Recognizing the contra-indication and dangers of cortisone therapy, we nevertheless gave it a trial. The results have been dramatic and singularly effective.

We mention at this time other effects of cortisone in addition to the relief of pain and disability of osteitis pubis. These patients are elderly with many of the degenerative processes incident to advancing age. It does not take much to accentuate their adrenocortical insufficiencies. The marked improvement in their sense of well being, the increased appetite and strength, and in general the impression of dealing with an altogether new patient are phenomena about which even the laity wonder. These changes have led us to use this therapy in other postoperative and preoperative cases in which we believed that the patient was slipping in spite of the usual methods of drainage, antibiotics, vitamins, fluid balance restoration and transfusions. So far we have not been disappointed.

SUMMARY

Osteitis pubis is a distressing and disheartening complication for the urologist.

Prompt, effective and lasting relief is afforded by a short course of cortisone therapy.

Other effects of cortisone noted in our treatment of osteitis pubis had led us to employ the drug in other cases characterized by adrenocortical deficiency with similar dramatic and effective results.

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CARCINOMA OF THE PROSTATE WITH UNUSUAL METASTASIS

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The following case report demonstrates an unusual metastasis from carcinoma of the prostate, and a very rapid and unusual response to the elimination of androgens.

REPORT OF CASE

C. G., aged 68, was examined on February 26, 1951. The patient complained of symptoms of prostatism of increasing degree over the past three to four months. For the past 4 months he had also noted progressive enlargement of his left leg including the thigh. He had had no episodes of acute retention of urine or hematuria.

Examination of the abdomen revealed a huge mass, hard and lumpy, most prominent in the left lower quadrant, but extending above the umbilicus into the left upper quadrant and was readily palpable in the right upper quadrant. This mass can be differentiated from the liver. Grade 4 pitting edema of the left leg and thigh and edema of the inguinal area were present. Collateral abdominal wall venous circulation was noted. The genitalia were normal except for absence of the right testis incidental to a previous herniorrhaphy. The rectal examination revealed an abnormal prostate, the left lobe of which was hugely enlarged and projected into the rectum. This lobe was softer than usual for carcinoma. Above this prostatic lobe, the main abdominal tumor mass could be palpated and there seemed to be a continuity of the prostate into the tumor mass. The urine was negative chemically and microscopically. X-rays of the chest were negative, and no invasion of the bones was demonstrated. The blood count showed mild secondary anemia. The nonprotein nitrogen was normal and the acid phosphatase revealed 0.4 Bodansky units.

Figure 1, *A* gives one an idea of the size of the abdominal tumor. Excretory urograms revealed a hydronephrosis grade 1, on the left with the ureter not filled in any of the studies. The right pyelogram showed an alteration in the normal configuration of the kidney with the pelvis away from the midline and the ureter bowed around the lateral extent of this tumor. The bladder was dislocated in the upper right segment of the pelvis.

A film taken after evaculation of a barium enema showed the displacement of the colon by the large tumor (fig. 1, *B*).

Biopsy revealed adenocarcinoma compatible with prostatic origin. On March 16, 1951, a transurethral resection of limited extent was performed through an external urethrotomy, and at the same time the remaining testis was removed. On this same day 5 mg. diethylstilbestrol by intramuscular administration was started. The prostatic tissue revealed extensive adenocarcinoma.

The patient was released from the hospital on the fifth postoperative day, and abdominal examination at this time revealed a remarkable diminution in the

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size of the abdominal tumor. The edema of the left leg was completely absent. Excretory urograms on the twelfth postoperative day (fig. 1, *C*) revealed shrinkage in the size of the tumor. At this time it was difficult to palpate the abdominal

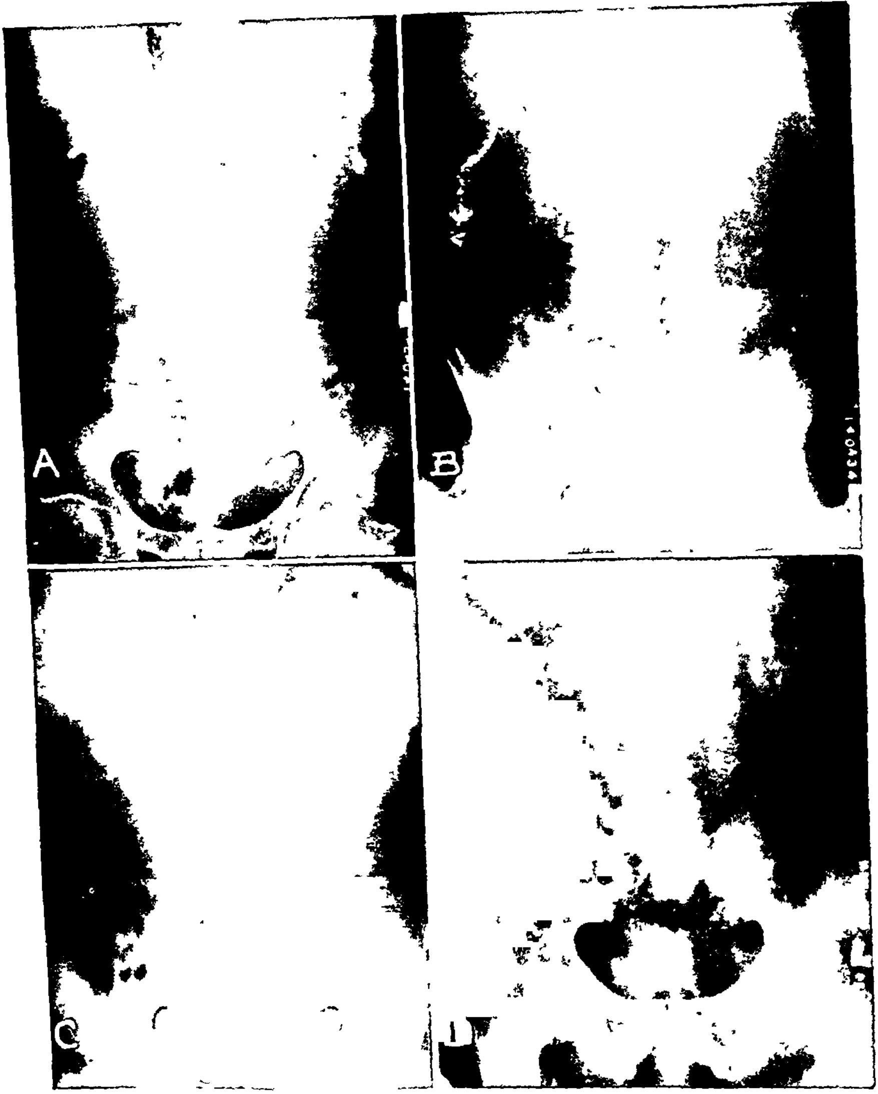

FIG. 1 *A*, excretory urogram *B*, after evacuation of barium enema; note extent of tumor when first seen *C*, excretory urogram 12 days postoperative *D*, excretory urogram 6 weeks after hormone treatment was commenced.

tumor, and the prostatic mass had reduced itself fully 40 per cent of its original size. The patient noted a marked increase in appetite. He had lost 10 pounds over the 12 day period, which was attributed mainly to the loss of tumor tissue. One month later, the abdominal and rectal examinations were considered normal by an independent observer.

The patient has remained well except for an episode of coronary occlusion on May 15. After recovery, another excretory urogram (fig. 1, *D*) showed that kidney function was normal. The psoas shadows were present and the cystogram was much more normally located.

SUMMARY

A case of carcinoma of the prostate with huge retroperitoneal metastases has been demonstrated. The remarkably rapid response to androgen alteration has also been described.

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RHABDOMYOSARCOMA OF THE PROSTATE

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Rhabdomyosarcomas of the urinary bladder or prostate occur chiefly in the male, and reviews of these tumors refer to the organ site of the growth despite the possibility that all may arise from a common tissue structure. Rappaport and Nixon stated that rhabdomyosarcomas are about 7 per cent of all sarcomas of the prostate. Khoury and Speers, in collecting the reports of these rhabdomyosarcomas, and with one of the urinary bladder that they described, listed nine of the urinary bladder and eighteen of the prostate. Kretschmer later collected sixteen published reports of rhabdomyosarcoma of the urinary bladder and included his patient who was one of two who survived beyond the usual duration of the disease. He listed in this group, a case reported by Hirsch and Gasser as originating in the urinary bladder. These authors, however, believed the tumor arose in the region of the prostate and it is so tabulated in our tabulation. Meisel, Heath and Miller in 1949 listed 23 patients with rhabdomyosarcoma of the urinary bladder and prostate. Of this number, 21 sarcomas arose in the region of the prostate and only nine in the urinary bladder. The other tumors were included with those arising from the urinary bladder.

Four rhabdomyosarcomas of the urinary bladder have been described in females. In both sexes, the ages ranged from 5 days to 69 years. All except five tumors of the urinary bladder had their origin in the region of the posterior wall or near the trigone and one was in a congenital diverticulum. Distant metastases occurred with three tumors which also had invaded the perivesicle structures. One tumor invaded the surrounding tissues but had not produced distant metastases. Rhabdomyosarcomas have been fatal within 13 months except one patient who survived for more than 4 years and another patient who was alive 6 months after the diagnosis had been made and at the time the description of his tumor was published. These patients had no recurrence or metastases at the time the reports were written.

The patients with rhabdomyosarcomas of the prostate range in age from 9 months to 79 years. Over 50 per cent were more than 20 years of age although 65 per cent were less than 40 years. The greatest incidence is the first decade. In this age group are nine of the 23 patients. Six tumors produced distant metastases and eleven invaded the surrounding structures. Only 1 patient survived longer than 13 months and had no evidence of tumor tissue 3 years after the initial diagnosis had been made.

Usually, obstruction of the bladder neck is the first symptom; sometimes hematuria, dysuria, fullness in the rectum, pain in the thighs and legs, acute retention, or tenesmus. The patient may also have an acute weight loss, anemia,

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TABLE 1. *Rhabdomyosarcoma of the urinary bladder*

NO.	YEAR REPORTED	REPORTED BY	SEX	AGE	POSITION	RESULTS
1	1907	Moncheberg	F	23 yrs.	Posterior wall of the urinary bladder	Expired
2†	1928	Mackenzie & Chase	F	69 yrs.	On the floor of the urinary bladder involving the entire trigone	Expired
3	1929	Houette	M	13 mos.	In a congenital diverticulum of the urinary bladder	Expired
4	1929	White	Not stated	22 mos.	Anterior wall of the urinary bladder	Not stated; prognosis poor
5	1933	Monserrat & Garcia	M	43 yrs.	Right wall of the urinary bladder	Expired
6	1936	Welfield, Hill & Hillebrand	F	Infant; not stated	Not stated	Expired
7	1936	Idem	M	24 mos.	Anterior wall of the urinary bladder	Expired
8	1939	Vermooten	F	20 mos.	Trigone	Expired
9	1939	Ratliff & Valk	M	6 yrs.	Entire bladder	Expired
10	1939	Idem	M	65 yrs.	Tumor attached to a pedicle 2 cm. above and to the left of the left ureteral orifice	Expired
11	1939	Uhlmann, Grossman & Calvin	M	10 mos.	Outer coat of the wall of the urinary bladder completely filling the space of Retzius. Mucosa apparently not involved by tumor	Expired
12	1943	Hunt	M	Newborn infant	Floor of urinary bladder; greater concentration around the neck	Expired
13	1943	Idem	M	2½ yrs.	Entire urinary bladder	Expired
14*	1944	Khoury & Speers	M	5 days	Floor of urinary bladder around the neck	Expired
15	1945	Buser	M	2 yrs.	Floor and posterior wall protruding through the mucosa	Expired
16	1945	Idem	M	5 yrs.	Trigone	Expired
17	1947	Minchen	M	17 mos.	Posterior wall of the urinary bladder	Expired
18	1947	Kretschmer	M	53 yrs.	Dome of the urinary bladder	Living 4 yrs. 2 mos. later
19	1947	Nahla	M	15 mos.	Posterior wall of the urinary bladder	Expired
20†	1948	Vipond	M	21 mos.	From pelvis (extraperitoneal)	Expired
21	1949	Meisel, Heath & Miller	M	32 yrs.	Posterior-lateral wall of the urinary bladder	Living 6 mos. later
22†	1951	Fister & Lund	M	10 mos.	Urinary bladder neck and posterior urethra	Expired

* Regional extension.

† Regional extension and distant metastases.

cachexia and by rectal examination an enlarged smooth hard, nontender prostate is found. In infants, exquisite tenderness may be present upon palpation of the lower abdomen, especially with distention of the urinary bladder, continuous priapism, and frequently irritability.

Radiation therapy is ineffective and seems to stimulate the tumor to a more rapid growth. Total cystectomy with transplantation of the ureters offers the best hope of cure. This procedure, however, must be instituted before the onset of hydro-ureters, hydronephrosis, pyelonephritis, systemic infections, and especially pneumonia.

TABLE 2. *Rhabdomyosarcoma of the prostate*

NO.	YEAR REPORTED	REPORTED BY	AGE	RESULTS
1	1902	Kaufman	9 mos.	Expired
2*	1902	Idem	4 yrs.	Expired
3†	1902	Idem	26 yrs.	Expired
4*	1908	Greig	4 yrs.	Expired
5*	1916	Squier	40 yrs.	Expired
6†	1926	Smith & Torgesen	31 yrs.	Expired
7	1926	Kretschmer	31 yrs.	Expired
8	1931	Katzman	13 mos.	Expired
9	1931	De Rom & Thomas	23 yrs.	Expired
10	1933	Urtubeg & Siere	59 yrs.	Expired
11†	1935	Foucar	26 yrs.	Expired
12*	1936	Lahayville & Diss	36 yrs.	Expired
13	1938	Katzen, Cohen & Steiner	2½ yrs.	Expired
14†	1938	Smith & Mintz	7 yrs.	Expired
15	1939	Stirling & Ash	79 yrs.	Living 3 yrs. later
16	1939	Idem	73 yrs.	Expired
17*	1939	Idem	53 yrs.	Expired
18*	1940	Taylor	55 yrs.	Expired
19	1944	Hirsch & Gasser	5 yrs.	Expired
20	1945	Rappaport & Nixon	20 yrs.	Expired
21	1947	Minchen	9 mos.	Expired
22†	1950	Mertz, Howell & Hammond	4 yrs.	Expired

* Regional extension.

† Regional extension and distant metastases.

All published reports of rhabdomyosarcoma of the urinary bladder and prostate are listed in tables 1 and 2. There are twenty-two each of the urinary bladder and the region of the prostate. Another rhabdomyosarcoma of the prostate region is described in this report, making a total of 45 cases.

CASE REPORT

A white male infant, aged 10 months, was admitted to the pediatric service at St. Luke's Hospital on January 30, 1951, with a 5 months' history of screaming when placed on his back, but comfortable when on his stomach or side; anorexia with solid foods of 3 months' duration; intermittent projectile vomiting usually following an automobile or street car ride, and hematuria for 2 months' duration; awakening at night and screaming, doubling over in agony with writhing and grasping of the lower quadrants of the abdomen for 3 weeks prior to admission; a rash on his face for 2 weeks; and diarrhea for 1 week. At the age of 1 month the patient had a severe throat infection from which he recovered promptly. Following this illness he had puffy, swollen eyelids and distention of the abdomen. Dysuria had been present since birth, indicated by grunting while voiding, and for the 2 months prior to admission, occasional crying spells accompanying the grunting.

Examination revealed an irritable, white, male infant refusing to lie on his back, with edematous eyelids, a urinary bladder distended to the umbilicus and normal external genitalia but with continuous priapism Rectal examination revealed the urinary bladder to be large, firm and pushing the rectum against the sacrum. The blood pressure was 110/60 mm. of Hg. and the temperature was 100.2F.

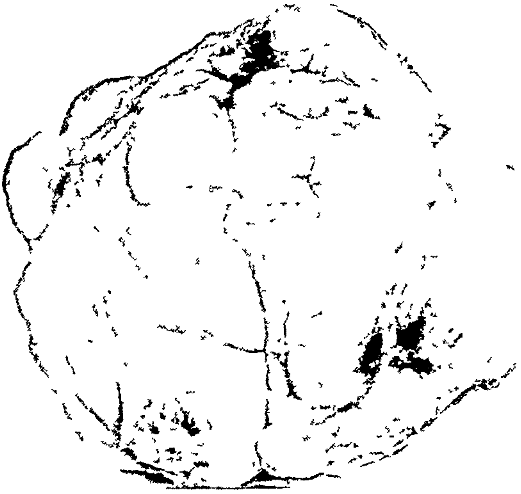

FIG. 1. Photograph illustrating surfaces made by hemisecting rhabdomyosarcoma

The laboratory findings were not unusual except for a blood urea nitrogen of 19.5 and a nonprotein nitrogen of 38 mg. per 100 cc. Roentgen films of the cranium were negative. A barium enema disclosed an extrinsic mass which displaced the urinary bladder upward and to the left of the descending colon. It was interpreted as being intrapelvic and possibly retroperitoneal. On the fifth hospital day, cystoscopy was attempted without success but a catheter could be passed and a cystogram revealed the urinary bladder to be displaced upwards and to the right of an abdominal mass which seemed to be extrinsic to the genito-urinary system. Two days later a suprapubic cystotomy was done by Dr. G. V. Pontius and a retrovesicle pelvic tumor was removed.

The ovoid tumor, 10.5 cm. by 7 cm. by 5 cm., weighed approximately 140 gm (fig. 1). Surfaces made by cutting were gray, coarsely lobulated, soft or slightly fibrillar and firm tissues. They had the consistency of a hyperplastic lymph node but with a different texture. A separate piece of torn capsular fibrillar tissue was

8 by 5 cm. and 1.2 cm. thick. One surface was hyperemic and the other surface was torn firm gray tissues. The histological examination established the diagnosis of rhabdomyosarcoma of the prostate (Edwin F. Hirsch).

A suprapubic drain was placed in the urinary bladder. One thousand r of radiation therapy was given to the anterior and posterior regions of the abdomen in 10 divided doses. The patient was discharged February 25, 1951, without improvement. On several occasions he was readmitted to the hospital for symptomatic care because the tumor recurred in the base of the urinary bladder. The child received another 1000 r to the anterior and posterior regions of the pelvis in 10 divided doses.

On July 16, 1951, he was readmitted to the hospital for the sixth time, having had four convulsions, and on the second hospital day following a convulsion, a mass of tumor tissue, small bowel and mesentery eviscerated through the cystotomy wound. Death occurred July 20, 1951.

The complete necropsy disclosed no metastases or extension of the tumor beyond the region of the prostate. A dark red, moderately soft, lobulated mass of tumor tissue 12 cm. by 11 cm. by 3 cm., protruded through the suprapubic cystotomy wound. It was attached to the posterior wall of the bladder neck by a broad pedicle composed of several yellow, gelatinous stalks ranging to 3 cm. The dilated right renal pelvis and ureter contained a turbid yellow fluid. The widest circumference of the right ureter in the midportion was about 4 cm. and below the renal pelvis it was 2.3 cm. There were foci of hyperemia in the distal 3 cm. of the lining of the rectum. The urethral orifice was not identified in the necrotic, yellow tumor mass. The ureteral orifices were demonstrated with a probe from the dilated upper segments of the ureters. There was a large growth of tumor and fibrous scar tissues around their walls where they entered the perivesical structures. The lining of the ureters was smooth and the walls were thin from distention. The lumen of the urinary bladder was exposed entirely to the external surface through the gaping cystotomy wound and approximately one-half of the lining surface was replaced by the large pedicle stalk which supported the friable, red tumor mass. The pedunculated base and stalk were composed of firm tissues. Arising circumferentially above the large pedicle were approximately 20 smaller pedunculated, gray-yellow gelatinous tumor nodules ranging to 4 cm. in length and 2 cm. in diameter. The large pedicle extended through the wall of the urinary bladder into the adjacent adventitial connective tissues. Behind and beneath the posterior wall of the urinary bladder was another large, soft necrotic and friable tumor mass approximately 7 cm. by 4 cm. by 3 cm. which filled the entire true pelvis. This tumor tissue on surfaces made by cutting was homogeneous, nongranular, soft and pale yellow. There were no invasions of the surrounding structures or distant metastases. The essentials of the anatomical diagnosis are: huge pedunculated and eventrated rhabdomyosarcoma of the prostate; old patent cystotomy wound of the abdomen; bilateral, obstructive hydronephrosis and hydro-ureters; focal fibrous peritonitis; focal hyperemia of the lining of the rectum; etc.

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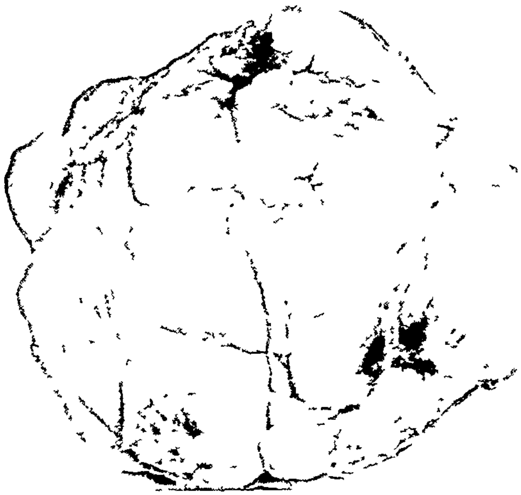

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The details of the histologic structure of both the surgical and autopsy tissues were alike. The capsular portions of the surgical material had dense fibrillar tissues in septums and between these were masses of cellular tissue, also fibrillar, with mesoblastic tumor cells, some spindle-shaped, a few pear-shaped. The masses of cells varied considerably in size and were not sharply separated from the supporting stroma. In these tissues, widely scattered were a few small tubules lined by columnar cells. Tissues from the main tumor mass also had fibrous septums separating masses of cellular tissue composed of atypical mesoblastic elements. Among the cells were many elongated or pear-shaped with fibrillar processes and large vesicular nuclei, and still others also round and large with one or several nuclei (fig. 2). Many cells were in mitosis. Among the cells were scattered large round forms with considerable cytoplasm and fine fibrils arranged concentrically (fig. 3, *C*). Further details of the structure of the tumor tissues were demonstrated in sections stained with phosphotungstic acid hematoxylin. These preparations had the general pattern of the tissue structure mentioned. The finer details were in the cellular portions. Here were spindle-shaped cells with fibrillar processes, cells with short bands of granular cytoplasm and large vesicular nuclei, segments of slender fibers with dark granules arranged like the light and dark bands of striated muscle fibers (fig. 3, *A* and *B*), large round cells with much granular cytoplasm and vesicular nuclei, and significantly, other even larger cells with concentrically arranged fibrils with dark granules like those in the fiber segments (fig. 3, *C*). These details and the purple staining qualities of the cells like muscle formed the basis for concluding that this cancerous tissue was a primitive form of rhabdomyosarcoma where the differentiation of cross striations was slight. The histological diagnosis of tissues from the various organs at autopsy was: recurrent rhabdomyosarcoma of the pelvis (prostate).

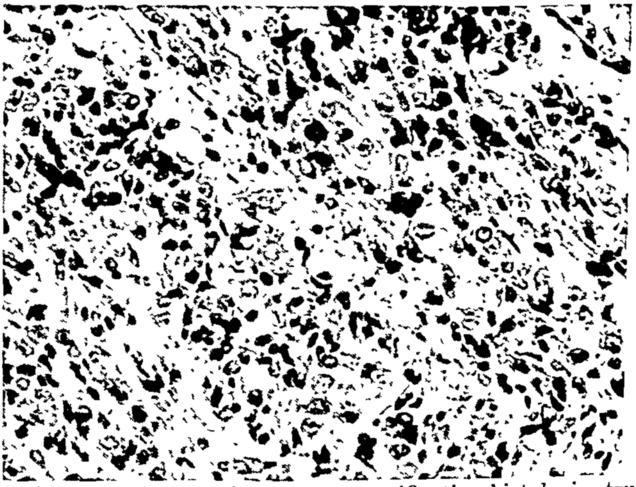

FIG. 2. Photomicrograph illustrating in low magnification histologic structure of tumor tissues. Note masses of large protoplasmic cells. × 198

Numerous authors have proposed that these tumors *arise in* striated muscle fibers normally present in the capsule of the prostate. This, however, *does not* adequately explain those tumors which are located some distance from the neck of the urinary bladder. Wilms expressed the opinion that in its caudal growth, the wolffian duct may leave displaced myotome tissues which later provide a nidus for the development of a rhabdomyosarcoma of the lower urinary tract. Gruenwald believed that two kinds of abnormal tissues may give rise to these tumors. The first are those tissues which originally are part of the primordium, become displaced and are found at a distance from the original site. The second are tissues with dormant potentials which later are stimulated to grow. This may explain the large number of tumors found in infants. The various cell forms characteristic of a rhabdomyosarcoma were found in the tumor of our report. Because the tubules observed in the capsular tissue resembled those of an immature prostate and the anatomical position of the tumor in the pelvis, the sarcoma is

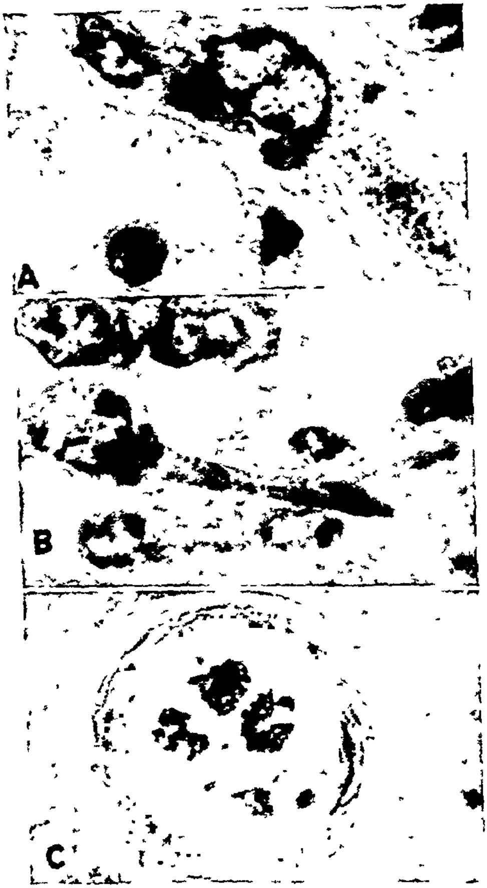

FIG 3. Photomicrographs illustrating oil immersion magnification of rhabdomyosarcoma cells *A*, cell with coarse cytoplasmic granules suggesting cross striations; *B*, more definite spindle-shaped cell with granules distributed in horizontal bands; and *C*, large multinucleated cell with concentrically distributed granular fibrils.

believed to have originated in the prostate. Buser reported two tumors with glands or tubule-like structures and concluded that they arose from displaced myotome elements as proposed by Wilms.

SUMMARY

A rhabdomyosarcoma originating in an immature prostate in a 10 months old male infant is reported. A review of the published reports reveals 22 rhabdomyosarcomas each of the urinary bladder and the prostate. The greatest age incidence is in infants and adolescents. At present surgery seems the best method of treatment. The tumors grow rapidly and usually are fatal. Only three patients survived a long time without recurrence after removal. Opinions differ as regards the genesis of these tumors, but the theory of aberrant germinal rests affords the most likely explanation, especially of those rhabdomyosarcomas of the genitourinary system which are somewhat removed from the neck or trigone of the urinary bladder.

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UTILIZATION OF SCROTUM IN RECONSTRUCTION OF PENIS

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During World War II, the Russians received extensive newspaper publicity for their reconstruction of the male genitalia. In 1944, Frumkin published a report of this work, which consisted essentially in the utilization of a tube of skin raised on the abdomen, and into which a segment of cartilage has been transplanted. The tube containing the cartilage is transferred in stages to the stump of the penis. The urethra is then constructed from a tube of scrotum or from a tube raised on the inner hairless surface of the arm and transferred in stages to the penis.

Several disadvantages of this technique are at once apparent. Loss of sensation in the transferred tube is the most outstanding disadvantage and would seem to obviate the advantages gained in most instances. The surgery required is very extensive, disfiguring and uncertain of success. Certainly in individuals with considerably body hair, it will be impossible to raise a hair free tube.

A method for utilization of the scrotum to obviate some of these disadvantages is presented.

TECHNIQUE

Parallel incisions are made on the anterior surface of the scrotum (fig. 1, *A*) utilizing as much of the scrotum as possible. This is easily determined by picking up the free scrotum in front of the testicles, leaving just enough scrotum behind to contain the testicles. The expected lines of incision can now be outlined. The upper limits of the incision extend above the base of the penis. The incision is deepened through the skin and cremasteric muscle but the tunica is not opened. The skin flap thus outlined is pulled aside and the skin separated from over the stump of the penis, exposing the stump of the corpora (fig. 1, *B*). The longest, thickest, straight segment of cartilage that can be obtained is taken from the costal margin; usually a segment the thickness of a rib and from 8 to 10 cm. long can be obtained. One end of the cartilage is trimmed to a wedge shape. An incision is now made into the stump of the penis between the corpora cavernosa and deep enough to accommodate the wedge shaped tip of the cartilage, preferably to a depth of 2 cm. It is probably advantageous to enter the corpora to secure free bleeding and possibly provide better nourishment for the cartilage graft. The stump of the penis is now closed about the cartilage with silk in such a manner as to fix the graft in place and to secure hemostasis. The cartilage is now slipped under the scrotal flap (fig. 1, *C*) and the scrotal tube containing the cartilage is now closed. The scrotal defect is also easily closed (fig. 2, *A*) and supporting dressings applied. After several weeks the distal end of the penile tube can be separated from the attachment to the scrotum. This can

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be done by a semi-circular incision so that the resulting scar will resemble the corona and give the cosmetic effect of a glans penis (fig. 2, *C* and fig. 3).

CASE REPORT

Mr. D. R. W., a 47 year old taxi driver, had an amputation of the penis in December 1948 for a grade 3 squamous cell carcinoma of the penis. The penis was amputated flush with the symphysis pubis and postoperatively there was contracture of the urethra with fibrosis and the urethral meatus was lost in the scar tissue of the stump of the penis. Two months postoperatively, I was asked to see patient because of his inability to void. The urethra could only be located by retrograde passage of sounds through a suprapubic cystostomy wound. A permanent urethrostomy was now done and although it was necessary to revise the urethrostomy opening on one occasion, it has continued to function satisfactorily. For the following 2 years, the patient was closely followed and there was no evidence of a reccurrence of the carcinoma of the penis although his mental status rapidly deteriorated and he became subject to a variety of imaginary ills, particularly those requiring narcotics and his addiction was prevented with difficulty. He repeatedly begged for castration to reduce his terrific sex desire. He adapted him-

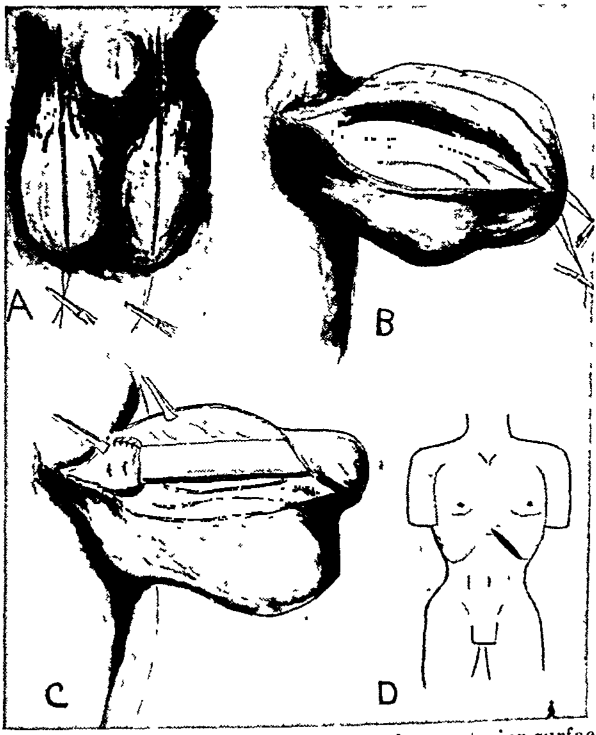

FIG. 1. *A*, proposed lines of incision are delineated on anterior surface of scrotum and extend above stump of penis. *B*, incisions have been made and scrotum incompletely divided into upper and lower halves. Testicles contained within tunica are seen to lie in lower half. Stump of penis is exposed. *C*, segment of cartilage has been fixed into split stump of penis with sutures and slipped under flap of skin formed by upper half of scrotum. *D*, site of incision for removal of cartilage from costal arch.

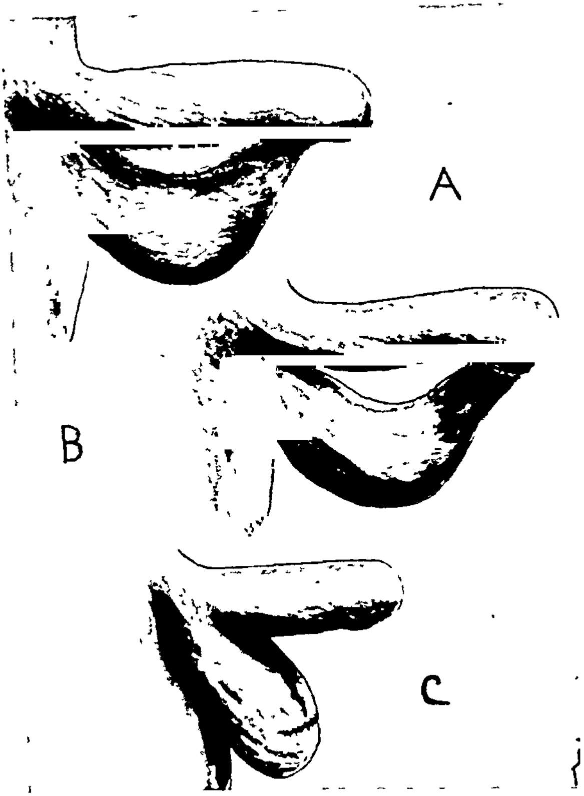

FIG 2. *A*, skin flap has now been sutured about cartilage implant and scrotum closed about testicles so that cartilage and testicles lie in separate compartments. *B*, line of incision for separation of new penis from scrotum. *C*, separation has been completed and wounds sutured.

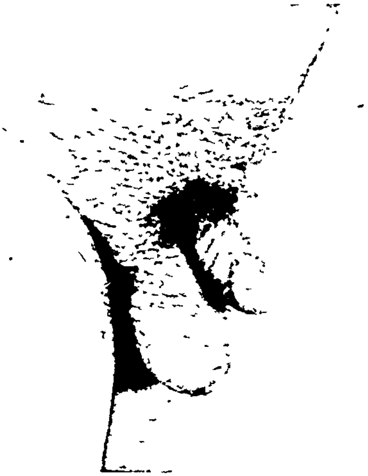

FIG. 3. Photograph of reconstructed penis 4 months after final surgery and shortly before patient was married.

self to his perineal urethrostomy without difficulty. In an effort to salvage the individual, he was promised that an effort to reconstruct his penis would be attempted. A reconstruction following the plan of Frumkin was first considered but patient was extremely hairy and a tube satisfactorily free of hair could not be raised. Because of this and the disadvantages above enumerated, the plan was abandoned and it became desirable for us to devise a more satisfactory and practical procedure. On January 24, 1951, a tube of scrotum was raised (fig. 1, *A*) utilizing all available free scrotum. A segment of cartilage 8 cm. long and the thickness of a rib was obtained from the right costal margin and was implanted into the stump of the penis and the scrotal tube closed about the cartilage (figs. 1, *C* and 2, *A*). A month later the distal extremity of the scrotal tube was separated from the scrotum (fig. 2, *B*) by a curved incision but unfortunately a sinus had developed on the undersurface of the penis at its base and there could be no healing of this sinus until there had been almost complete dissolution of the transplanted cartilage. Six months after the initial operation the patient was again subjected to surgery. The scar in the skin of the dorsal surface of the reconstructed penile tube and representing the old amputation scar was excised and only a very small fragment of cartilage found remaining. The sinus on the ventral surface was now excised and the wound closed in several layers, both from the inside using chromic catgut and from the skin side with silk. A larger (10 cm. by rib thickness) piece of cartilage was obtained from the left costal margin and implanted into the base of the penis, the stump of the penis being split to receive the end of the cartilage and the cartilage fixed to the stump of the penis with several silk sutures. The dorsal skin wound closed with silk and a supportive dressing applied. Healing was without incident, he was allowed to go home three weeks after surgery and one month later successfully had sexual intercourse. The act was normal and ejaculation occurred. The only complaint was that the orgasm occurred much sooner than before his amputation. Patient felt so confident of his sexual ability that he married in early November 1951. His married life has been satisfactory thus far. The penis ordinarily hangs in a semi-rigid state that permits easy wearing of clothing; with sexual stimulation it becomes more rigid and erect due to filling of the stump of the corpora.

COMMENTS

The technique just described has many faults and has not been proven by time or number. It is believed that it is so simple as to be entirely practical and that it offers advantages over previously described methods. The fate of the cartilage will of course determine the true value of the procedure. Reconstruction of the urethra, while not done in this case, is as practical here as in the other methods of reconstruction. Many modifications offer themselves at once and will of course make the procedure adaptable to a number of plastic reconstructive procedures. For example, in incomplete amputations, a short stump could easily be lengthened. Other refinements of technique such as use of two pieces of cartilage may increase the value of the operation.

SUMMARY

A method for reconstruction of the penis from a tube raised from the scrotum with cartilage implants is presented. A case of amputation of the penis at the symphysis pubis that had a successful reconstruction and in which the patient was married 4 months after surgery is presented. While many faults are admitted, it is believed that the technique herein presented is simple, practical, and superior to previous techniques.

The author wishes to publicly thank Drs. Tom Ellis and George Bunch for the obtaining of the cartilage segments and thus contributing significantly to the success of the surgery.

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CYSTIC LYMPHANGIOMA OF THE SCROTUM

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Cystic lymphangioma of the scrotum, which may be confused with hydrocele of the tunica vaginalis testis, can be successfully treated by surgical excision. This tumor characteristically has its origin in the dartos tunica of the scrotum, is intimately adherent to the scrotal wall and therefore offers greater difficulty to surgical removal. The two disease entities can be differentiated by ordinary physical examination.

Five similar cases have been reported in the literature. All of these were treated by surgical excision. This paucity of reported cases might indicate that cystic lymphangioma of the scrotum is of infrequent occurrence. The fact, however, that the authors have seen two patients with this disease in a short period of time raises the question as to whether or not this tumor occurs with greater frequency than is recognized, or at least reported.

CASE REPORTS

Case 1. K. D. S. No. 125923, a 3½ year old boy, was admitted to St. Joseph's Hospital on February 7, 1951. At the age of 6 weeks the mother had noticed that the skin of the right half of the scrotum was more abundant than that of the left and was thrown into folds. At the age of 2½ years the right scrotum began to enlarge, attaining the size of an orange within several weeks. The family physician attempted aspiration of the mass but only a few drops of fluid were obtained. Four days later the scrotum and perineum were found to be discolored bluish-black. This gradually disappeared during the ensuing weeks. During the year preceding hospitalization the mother had noticed that the right buttock seemed larger than the left. The child never complained of pain or tenderness in the scrotal or perineal areas.

On examination the right side of the scrotum was enlarged, being 10 by 7 by 6 cm. in diameter. Several dilated, tortuous veins were visible beneath the skin. The surface of the mass was nodular and cystic and there were several areas of bluish discoloration. The skin seemed fixed to the underlying mass, which could be transilluminated. The testes and spermatic cords were palpable, normal in size and consistency. On the upper anterior aspect of the right side of the scrotum there was a 1 cm. area of induration which was adherent to an almond-sized, firm, non-tender mass beneath. This was presumably the site of previous aspiration. There was a distinct prominence of the right half of the perineum and the gluteal fold on the right was 3 cm. lower than on the left. Digital examination of the rectum revealed no abnormalities. Preoperative diagnosis: Multiple cystic mass of the right scrotum of undetermined type.

On February 8, 1951 excision of the right scrotal mass was carried out. An incision 6 cm. in length was made through the skin on the anterior-lateral aspect of

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the right scrotum. Exploration revealed a mass composed of numerous cysts varying from several millimeters to several centimeters in diameter. It was intimately adherent to the skin, the shaft of the penis and to the scrotal septum. It extended into the inguinal region superiorly and into the ischiorectal fossa inferiorly. Just below the testis there was a firm cyst 2 cm. in diameter which appeared to contain a thick chocolate-colored material. No cleavage plane could be found between the mass and adjacent structures, and it could be separated only by scalpel dissection. In so doing many cysts were opened and remnants of the cyst walls were left behind. The testis and spermatic cord were easily dissected free. The tunica vaginalis testis was opened. There was no hydrocele and the testis and the epididymis and spermatic cord appeared normal. The wound was closed leaving a rubber tissue drain which was brought out through a stab wound near the scrotal-perineal juncture.

The wound healed well and the patient was discharged on the eighth postoperative day. The patient did not return for examination for 9 weeks, and then was found to have an infectious eczematoid dermatitis of the right side of the scrotum, which later responded well to treatment. He was last seen 9 months postoperatively, at which time the right side of the scrotum was redundant and the wound well healed. There was no evidence of recurrence of cysts.

Case 2. W. D. No. 115308, a 13 year old white boy, was admitted to St. Joseph's Hospital on April 17, 1951. The father stated that when the child was 5 years old he noticed a dime-sized area of bluish discoloration on the under aspect of the right side of the scrotum. At the age of 10, an egg-sized mass was visible and palpable in the right half of the scrotum. About 6 months prior to admission the mass suddenly increased in size. One month later the boy began to complain of a dull, aching discomfort in the right scrotal region associated with tenderness but no discoloration.

On examination the right side of the scrotum was enlarged to about 10 by 8 by 6 cm. in size (fig. 1). The skin was normal in color but seemed fixed to the underlying mass, which could be transilluminated. The surface of the mass was irregular and cystic. Both testes and cords were palpable and seemed normal in size and consistency. The inguinal and perineal areas were normal to examination. Digital examination of the rectum revealed no abnormalities. Preoperative diagnosis: Cystic lymphangioma of the scrotum.

Surgical excision was carried out on April 18, 1951. An incision was made through the skin on the anterolateral aspect of the right side of the scrotum. As in the previous case, the tumor was found to consist of numerous thin-walled cysts filled with light yellow fluid and varying in size from several millimeters to several centimeters. The tumor mass was intimately adherent to the skin, scrotal septum and base of the penis. It extended from the inguinal region to the scrotal-perineal junction. During removal of this mass no line of cleavage could be established and excision was accomplished by scalpel dissection. Again remnants of the cyst walls were left behind. The tunica vaginalis testis and spermatic cord were easily separated from the tumor and upon opening the former the testis and epididymis appeared normal. The wound was closed with dependent drainage.

The postoperative course was uneventful. The wound healed well and the patient was discharged from the hospital on the eighth postoperative day. Examination 7 months later revealed mild redundancy of the right scrotal skin. The testes and spermatic cords were normal to palpation and there was no evidence of recurrence of cysts within the scrotum.

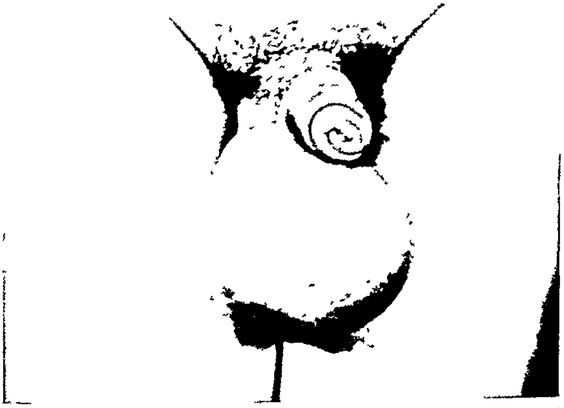

FIG. 1. Case 2. Appearance of lesion before surgery. Appearance of lesion in case 1 was identical.

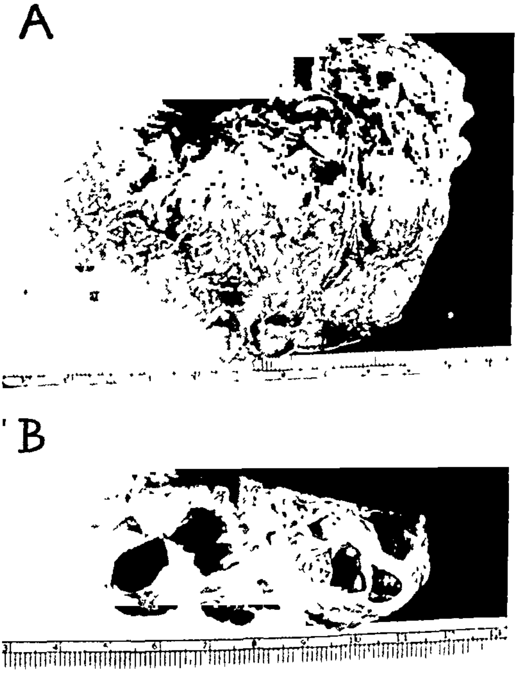

FIG. 2. Case 2. *A*, lobular and multicystic appearance of uncut specimen. *B*, appearance of specimen on cut section showing multicystic nature of tumor.

Pathological examination: Both specimens were remarkably similar in appearance. The one from the first case consisted of an irregular cystic mass 9 by 3 cm.

as well as some smaller fragments of cystic tissue. The surface was somewhat smooth and on palpation felt lobular (fig. 2, *A*). On section the entire mass was found to consist of cystic spaces measuring from a few millimeters to 2 cm. in diameter (fig. 2, *B*). The walls were generally thin, although deep in the mass the walls were composed of rather dense fibrous tissue. The lining of the cysts was smooth and the cysts were filled with a slightly milky, thin fluid. One of the cysts contained chocolate-brown viscid material.

The specimen from case 2 was similar in appearance. It measured 9 by 8 by 4 cm.

Microscopically the cysts were found to be lined by endothelium. The cyst walls were thin but in some sections were surrounded by dense fibrous tissue in which were found bundles of smooth muscle (fig. 3). A small amount of scattered infiltration with mononuclear cells was present but this was not a prominent feature. The cyst containing the chocolate-brown material showed phagocytic cells filled with blood pigment in the wall. Pathological diagnosis: *Cystic lymphangioma of the scrotum.*

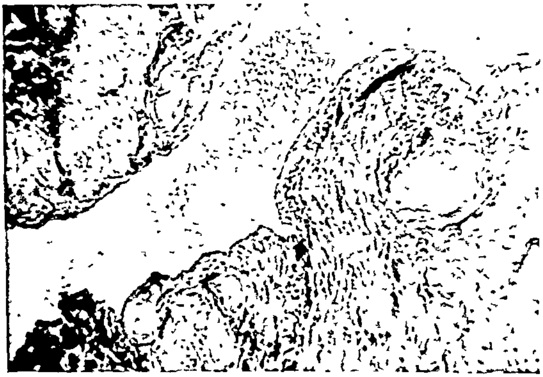

FIG. 3. Photomicrograph showing cystic spaces lined with endothelium and bundles of dartos muscle in walls.

The appearance of the sections was similar to the appearance of a cystic lymphangioma occurring elsewhere with the exception that in both specimens bundles of smooth muscle, probably representing dartos muscle, were prominent features. Because of this finding, it is felt justified to conclude that the lymphangioma arises from the scrotum proper. Although it is impossible to be sure from the morphology alone, it was believed that this was a true cystic lymphangioma arising as a new growth rather than from dilatation of lymphatic spaces. The absence of endothelial proliferation indicates the essentially benign nature of the tumor.

DISCUSSION

The cases previously reported are remarkably similar to ours. Loffler reported a case of a 22 year old man who had noted a small nodule in the scrotum since childhood. Three weeks prior to examination it suddenly became tender and enlarged rapidly, attaining the size of a hen's egg. One portion of the tumor gave a bluish discoloration to the overlying skin. The diagnosis of a cystic tumor of the scrotum was made. Excision under local anesthesia revealed the tumor to be markedly adherent to the skin and to the scrotal septum. The excised specimen was found to be a multicystic tumor composed of thin-walled cysts containing serous fluid, which varied in color from light yellow to reddish brown. On section the cysts were found to be separated from each other by septa.

On histologic examination it was apparent that the tumor lay in the dartos tunica. There were large spaces separated by septa of varying thickness and lined by endothelium. Muscular fibers of the dartos tunica were scattered throughout and there was a slight amount of lymphocytic infiltration. Some of the cysts contained blood.

Haslinger reported a case occurring in a 19 year old boy. The tumefaction occurred suddenly without known antecedent trauma. It seemed multiloculated and fixed to the overlying skin. Surgical excision was carried out. The mass was composed of many cysts varying from cherry size to plum size, was intimately adherent to the scrotal skin, did not involve the testes or spermatic cords and extended into the perineal region and along the shaft of the penis. Cut section revealed many cysts which did not communicate, and which were separated by connective tissue strands. Microscopically the cysts were filled with a clear homogenous material containing many lymphocytes. Some of the cysts were filled with old blood. The cyst walls were lined with a single layer of epithelial cells. Between the cysts there were strands of fibrous tissue containing many blood vessels and dilated lymph spaces. No mention was made of recurrence following excision. The author included in his article brief résumés of a similar case reported by Frank and another by Rosenberger.

Bouteau and Dubarry described a case of lymphangioma of the scrotal septum occurring in a 24 year old man. Apparently this had appeared following an injury 20 years previously and three weeks prior to examination had become tender. Examination discosed a polycystic mass the size of a small tangerine arising from the scrotal septum. The overlying skin was normal in color and appearance save for an area of bluish discoloration posteriorly. The mass was excised. On cutting the fixed specimen it was seen that the peripheral area was composed of cysts containing serous fluid, separated by septa of connective tissue. The central areas had the appearance of corpus cavernosum having a vascular pattern similar to sinusoids. Histologically sections showed a "vascular angioma" with thick walls containing numerous smooth muscle fibers.

Other authors have described cystic lymphangiomas arising from intrascrotal structures such as the spermatic cord (Rosenfeld, Ormond and Culp) and the tunica vaginalis testis (Foged). These apparently did not have their origin in the scrotal wall or septum as did the above cases and did not contain smooth muscle fibers in the septa between the cysts. It seems justified, therefore, to limit the diagnosis of cystic lymphangioma of the scrotum to tumors which are intimately associated with the smooth muscle of the dartos tunica.

The two predominant features which serve to differentiate this tumor from hydrocele of the tunica vaginalis testis on physical examination are: 1) the irregularity of surface contour due to the presence of numerous cysts of varying diameter, and 2) the intimate adherence of the cystic mass to the overlying skin.

SUMMARY

Cystic lymphangioma of the scrotum can be successfully treated by surgical excision and can be differentiated from hydrocele of the tunica vaginalis testis by ordinary physical means. This tumor is thought to have its origin in the dartos tunica of the scrotum. We believe that only five cases have been reported in the literature. To these we add two.

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THE UROLOGICAL IMPORTANCE OF RADIOPAQUE APPENDICEAL CONCRETIONS

GEORGE C. PRATHER AND JAMES A. SINGISER

Opaque and nonopaque appendiceal concretions have long been recognized by the radiologist and pathologist. In 1813, Wegeler described appendiceal concretions, and as early as 1906, Weisflog noted radiopaque appendiceal concretions. Since that time, over one hundred reports on this subject have appeared in the medical literature.

Despite the rather widespread interest in appendicoliths, we know of no papers on this subject in the urological literature. Most modern textbooks of urology mention briefly appendiceal concretions as one of the many possibilities to be considered in the differential diagnosis of ureterolithiasis. It is the purpose of this paper to re-emphasize the urological significance of these concretions and to report three illustrative cases.

The differential diagnosis between acute appendicitis and ureterolithiasis is a frequent problem and often requires urological opinion. The clinical picture may be bizarre and the diagnosis uncertain. If the roentgenogram shows an area of opacity in the region of the right ureter, it becomes the responsibility of the urologist and radiologist to determine its significance, location, and the advisability of further study. The most common causes for areas of increased radiological density in this region are: ureteral calculi, phleboliths, arteriosclerotic placques, calcified mesenteric glands and artefacts. Over twenty other conditions produce abdominal calcifications, but most of these, with the exception of cholelithiasis and accompanying cholecystitis, are not commonly associated with an acute inflammatory process and serious consequences are not attendant upon incorrect interpretation.

The lower right ureter is in close proximity with the cecum, and disease of one structure may simulate that of the other. This phenomenon is especially true of appendiceal concretions and ureteral calculi where even the radiological appearance may be seemingly identical. Mark and Seelig have each reported a case of appendiceal stone with symptoms of ureteral colic, dysuria, frequency of urination, microscopic hematuria and an opacity along the course of the lower right ureter. Upon retrograde catheterization of the right ureter in both instances, obstruction was met at the site of apparent calcification and a diagnosis of ureteral calculus was made. In both patients the preoperative diagnosis proved incorrect, and at surgery, an acutely inflamed, retroperitoneal appendix with concretions was found. The concretions discovered in the surgical specimens corresponded exactly to those noted in the preoperative x-ray film. The appendix was intimately adherent to the ureter and provoked symptoms of ureteral colic; in addition, it caused obstruction of the ureteral catheter. Both cases were completely relieved of their urological symptoms by appendectomy. Conversely, Mathé states that 25 per cent of patients with right ureteral calculi in a series

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of 122 cases had been erroneously operated upon for appendicitis or pelvic disease.

The clinical significance of early and accurate diagnosis becomes increasingly important when it is realized that appendicitis complicated by concretions is associated with a higher morbidity than appendicitis alone. Childe reported a 37.5 per cent incidence of perforations in eight children with appendiceal concretions. Thomas found that there were four perforations in the 6 cases which he studied, or 66.6 per cent. Felson and Bernhard reported perforation in 47 of 99 patients in whom appendicoliths were found at operation. In 19 of their cases, perforation resulted in abscess, and in 10 there was a diffuse peritonitis. Therefore, the recognition and diagnosis of appendiceal concretions is not merely of academic interest. Even as an incidental finding in the asymptomatic patient, it should alert the physician to the possibility of future complications.

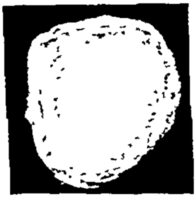

FIG. 1

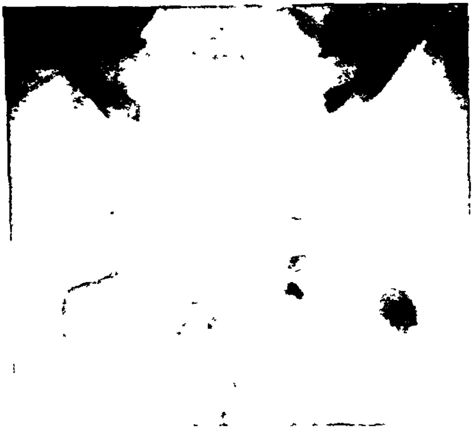

FIG. 2

FIG. 1. Enlarged x-ray of opaque appendiceal stone showing lamination
FIG. 2. X-ray of bony pelvis showing laminated, ring-like appendiceal concretion.

ETIOLOGY

The etiology of appendiceal concretions is a matter for conjecture. They may form entirely within the appendix or develop from foreign bodies which have passed from the bowel into the appendix. Some investigators maintain that all appendicoliths were once true enteroliths. There is no portion of the appendix which has a predilection for appendicolith formation. Their role is important in obstructive appendicitis; and perforation, when it occurs, is always distal to the concretion.

PHYSICAL CHARACTERISTICS AND CHEMICAL COMPOSITION

Appendicoliths vary in size from less than one millimeter to huge concretions measuring 3–4 cm. in diameter and weighing 13.5 gm., as reported by Pilcher. The average size is approximately 0.5 cm. The surface is usually smooth and the shape is generally oval, cylindrical or round. Single concretions are found in about two-thirds of the cases. Lamination is commonly present and is one of the diagnostic features when visualized by x-ray (figs. 1 and 2).

Maver and Wells analyzed several groups of concretions and discovered that: 25 per cent of the total weight was inorganic material, chiefly calcium phosphate; 20 per cent was organic residue, mostly vegetable fibers; and that the remaining 55 per cent was composed of soaps, cholesterol, and coprosterol.

The final consistency of any appendicolith will depend, of course, upon its chemical composition. Usually, the older concretions are harder and more opaque from greater deposition of inorganic salts.

INCIDENCE

Accurate figures as to incidence cannot be given. Graham and Guthrie report the general incidence of fecoliths in the appendix (calcified and noncalcified) as 18 per cent. Aschoff totalled both types at 60 per cent, and Steinert, et al., found 10 examples of radiopaque concretions in 104 appendectomies, or an incidence of 10 per cent. Felson and Bernhard encountered 10 patients with radiopaque appendiceal concretions in a series of 300 appendectomies. Eight of these cases were verified at operation with an incidence of about 3 per cent. They also observed in their review of the literature that of the 60 patients whose sex was mentioned 47 were males and 13 were females. This male preponderance conforms with the sex ratio seen in acute appendicitis. Twelve of the patients were in the second decade; 21 in the third; and 15 in the fourth.

DIAGNOSIS

It is not the purpose of this paper to present an elaborate discussion of the numerous opacities in an x-ray film of the abdomen which theoretically might be confused with appendiceal or ureteral calculi.

The possibilities are quickly narrowed to a few probabilities by considering the number, size, shape, outline, distribution, density and bilateral conformity of the calcifications, together with previous history of medication, disease or injury.

In some instances, third dimensional studies may be required. Stereoscopic, lateral and oblique x-ray films may be sufficient to localize the opacity in the abdominal wall, abdomen, or the retroperitoneal space. If the diagnosis remains in doubt and the patient's condition permits, retrograde pyelography or excretory urograms are indicated.

There is great variation in the anatomical position of the appendix. The greatest percentage of appendiceal concretions will appear within a 15 cm. radius of the midpoint of the wing of the right ilium. An appendix containing concretions may be mobile or fixed depending upon the degree of inflammation present. When there is mobility, calcified mesenteric lymph nodes may confuse the diagnosis; however, the latter are usually multiple, rougher in outline and are seen along the insertion of the mesentery in a line drawn from the ileocecal area to the splenic flexure.

In exceptional cases, it will be necessary to utilize the entire gamut of roentgenographic procedures to identify an area of opacity. Three cases are presented to emphasize some of the features already stressed.

CASE REPORTS

Case 1. A doctor's son, aged 14 years, complained of right flank and right abdominal pain. The urine was said to contain pus cells so that sulfadiazine was given to the boy by his father for 2 days. Pain continued and a temperature of 99.6–100.2F developed. Another urine examination showed many red corpuscles in the sediment. An x-ray film of the abdomen disclosed an opaque shadow in the course of the right lower ureter suggestive of calculus. A retrograde pyelogram in anteroposterior and right oblique positions demonstrated the opaque shadow in immediate proximity to the ureter (figs. 3, *A* and *B*). Only with additional films could a stone in a ureteral diverticulum be ruled out (figs. 3, *C*). Barium enema demonstrated the opaque shadow in the appendix (fig. 4). Appendectomy confirmed the diagnosis of appendiceal stone.

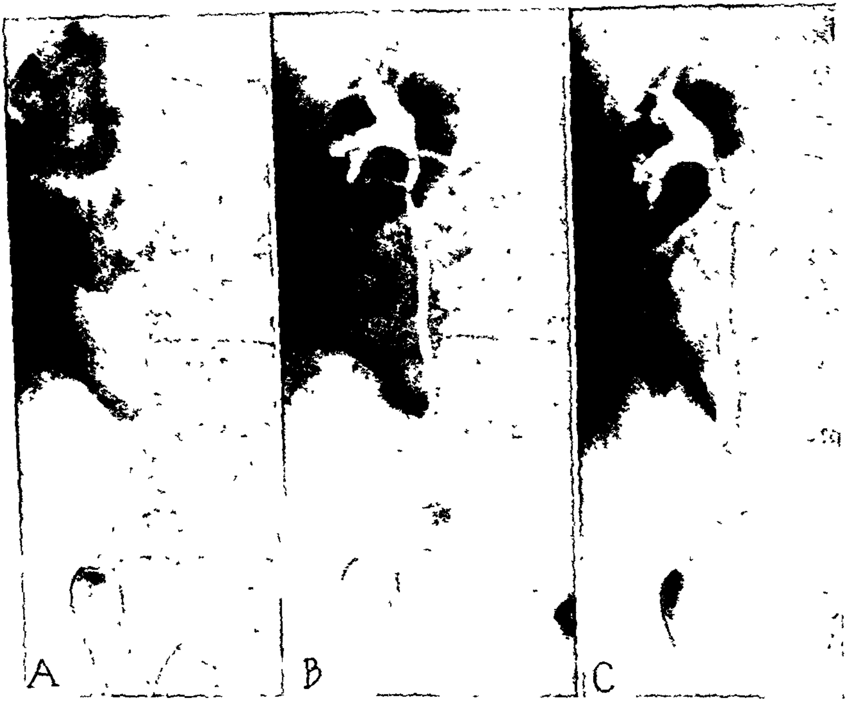

Fig. 3. Case 1. A, scout film showing smooth opaque shadow over right sacrum in line of right ureteral catheter. *B*, retrograde pyelogram showing opaque shadow still in line of ureter although there is no dilatation of upper ureter. Calculus in ureteral diverticulum could not be ruled out by this film. *C*, retrograde pyelogram showing opaque shadow separated from ureter. Appendiceal stone has fortunately changed position.

Case 2. A white man, aged 35 years, entered hospital complaining of sharp para-umbilical pain and diarrhea of several hours' duration. Shortly thereafter, nausea and vomiting developed and his pain shifted to the right flank. The patient also described increased frequency of urination and a burning sensation in the glans penis.

Past history was of interest because the patient had been on the urological service 3 years previously for urinary tract infection, at which time an excretory urogram revealed a rounded opaque shadow 1 cm. in diameter overlying the tip of the right twelfth rib, definitely extrarenal in location.

Physical examination on subsequent hospital admission disclosed diffuse tenderness over the entire right side of the abdomen, right costovertebral tenderness and point tenderness in the flank. Peristalsis was reduced to a few high pitched sounds.

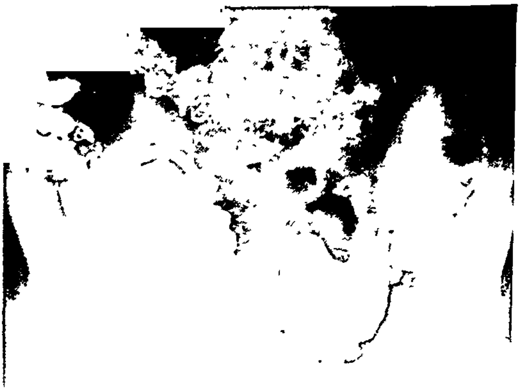

FIG. 4. Case 1. Barium enema demonstrates appendix containing opaque concretion.

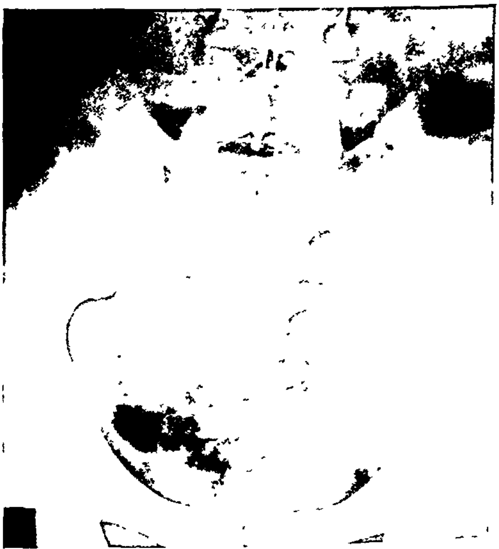

FIG. 5. Case 3. Scout film showing opaque calculus in line with right ureter. Ruptured appendix and appendiceal calculus removed by surgeon.

Temperature was 99.4F; pulse, 90; and respirations, 20. White blood cell count was 12,500. Urine sediment showed 15 red blood cells per high power field. X-ray examination again showed the opaque shadow seen in films three years previously. The preoperative diagnosis was appendiceal stone.

The surgical service removed an acutely inflamed retrocecal appendix which contained the hard opaque concretion in its middle third.

Case 3. A man, aged 44, was admitted to the hospital because of abdominal pain of 36 hours' duration. During this time, the pain had become localized in the right flank. Temperature of 103F had been present for 24 hours.

Past history revealed acute nephritis 20 years previously. This disease had been followed by hypertension and albuminuria.

Examination disclosed a temperature of 101F, pulse 92 and respirations 22. Blood pressure was recorded as 170/94. Abdominal palpation revealed localized tenderness and spasm in the right lower quadrant of the abdomen and the right flank.

White blood cell count was 16,000. The urine showed a 2 plus albumin with 35 red blood cells per high power field in the sediment. An x-ray film of the abdomen showed an opaque shadow in the normal course of the lower right ureter (fig. 5) but the excretory urogram did not indicate any delay in secretion by the right kidney or any hydronephrosis consistent with renal type of pain.

Although the surgeon who had seen the patient believed appendicitis a likely diagnosis, he favored ureteral stone with urinary infection because of the urinary sediment and the disclosure of the x-ray. One of us who saw this patient did not believe the x-ray studies indicative of ureteral stone and considered the urinary findings consistent with chronic nephritis.

The surgeon removed a ruptured appendix.

Retrograde study following appendectomy failed to show an opaque shadow or ureteral obstruction.

DISCUSSION

Because of the tendency of appendiceal stones to aggravate inflammation distal to the stone and thereby to create a surgical emergency, an immediate and accurate diagnosis is important. Urological study by stereoscopic and oblique pyelograms may be required to rule out ureteral stone and will be less hazardous in aggravating the abdominal condition than barium enema. Furthermore, should barium enema be done first with an inconclusive result, urological study would necessarily be delayed until the intestine has been cleared of opaque material.

Opaque appendiceal concretions should be known to all physicians as a condition which can be confused with ureteral calculi.

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PERIRENAL AIR INSUFFLATION BY PARACOCCYGEAL METHOD

SAMUEL H. ROTHFELD, FRANK C. HAMM AND HARRISON C. HARLIN

Perirenal air insufflation as a method for determining the size and shape of the kidney was introduced in 1920 by Carelli. Untoward reactions such as air emboli, pneumothorax, paroxysmal coughing, led to discontinuance of the procedure. Cahill, in his investigation of adrenal tumors, reintroduced the injection of air into the perirenal tissues.

In the technique of lumbar perirenal insufflation, the patient lies in the lateral recumbent position. After surgical preparation, a lumbar puncture needle is inserted at a point two finger breadths below the twelfth rib and two finger breadths lateral to the erector spinae group of muscles and directed upward and inward toward the kidney. About 500 cc of the medium is permitted to flow into the perirenal space through a pneumothorax machine. The disadvantages of this procedure have been: 1) unilateral visualization; 2) increased respiratory distress because of the patient's position, 3) air embolus and 4) pneumothorax.

We are convinced that perirenal air insufflation is of value in determining the size and shape of the kidney when parenchymal disease is suspected or exists. In the diagnosis of enlargement of the adrenal gland, it is a valuable adjunct. Perinephritic disease, displacement of the kidney and retroperitoneal tumors have been visualized by this method. More recently, this procedure together with translumbar aortography has been of inestimable value in the determination of renal tumors, cysts, and other pathologic entities.

In the past two years at the Brooklyn Veterans Administration Hospital, we have modified Rivas' technique of perirenal air insufflation by the paracoccygeal route. This permits simultaneous bilateral introduction of the medium. It is simple, without danger and requires only the use of the following material:

10 cc of 1 per cent novocaine
1 10 cc syringe, a hypodermic needle and a No. 20 1½ inch needle
1 No. 18 gauge spinal needle
1 50 cc syringe
1 three-way valve
6 inches of pressure tubing with absorbent cotton for air filtration

In the adult (fig. 1, *A*), the urinary bladder lies in the anterior lower part of the pelvis; in infancy partly in the abdomen also. The superior surface is covered with peritoneum except in the male, a small part of the base, from which it is reflected on to the rectum. In the female, the peritoneum is reflected from the posterior border of the superior surface of the bladder on to the uterus at the junction of the cervix and body. The ureters enter the posterior angles of the superior surface. In their course from the kidneys, they are immediately under

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cover of peritoneum until they approach the bladder. The rectum, which is approximately 5 inches long, begins at the middle portion of the sacrum, follows the curve of the sacrum and coccyx and ends an inch beyond the tip of the coccyx on a level with the apex of the prostate by bending backwards to become the anal canal. Peritoneum covers the anterior surface and sides of the upper third, covers the anterior surface of the middle third and is reflected on to the bladder or vagina, forming the bottom of the rectovesical or rectovaginal pouch, about an inch above the base of the prostate in the male. It is evident that the lowest third of the rectum is below the level of the peritoneum, imbedded in fat and fascia. In this area, there are no important blood vessels or nerves which may be entered or injured by the procedure to be described. It is in this area that the tip of the needle is placed. Thus, there is no danger of pneumothorax or air embolus. Respiratory embarrassment is avoided by the position of the patient.

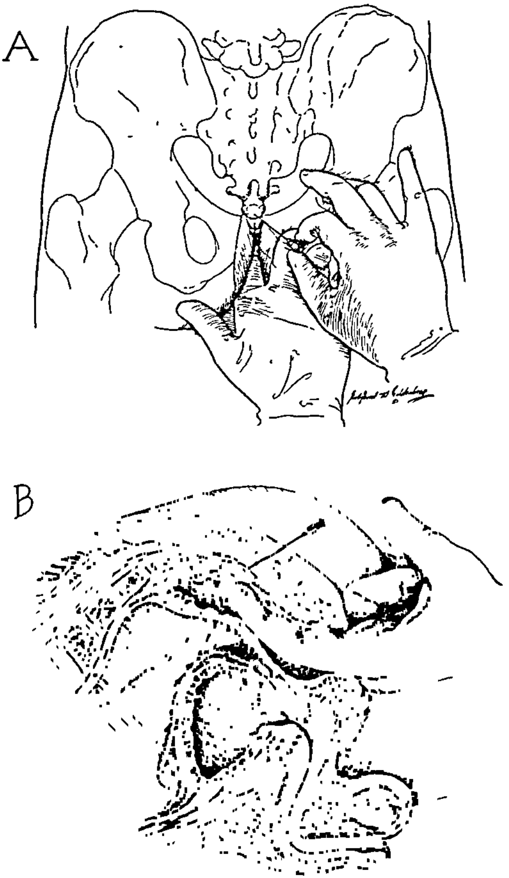

Fig. 1. *A*, needle in place for perirenal air insufflation. Note its position between coccyx and rectum. *B*, position of needle as seen anterior to coccyx (sagittal view).

PROCEDURE

Aseptic technique is employed at all times. The patient is placed in the prone position. After shaving the sacro-coccygeal area and the buttocks, phisoderm and aqueous metaphen are applied. The index finger of the left hand (in a right handed individual) is placed into the rectum, the tip of the digit being above the base of the prostate or at approximately the midcoccyx. Gentle pressure is applied to the posterior wall of the rectum in order to palpate the point of the needle and the crepitus of the injected medium at all times. See figure 1, *B*.

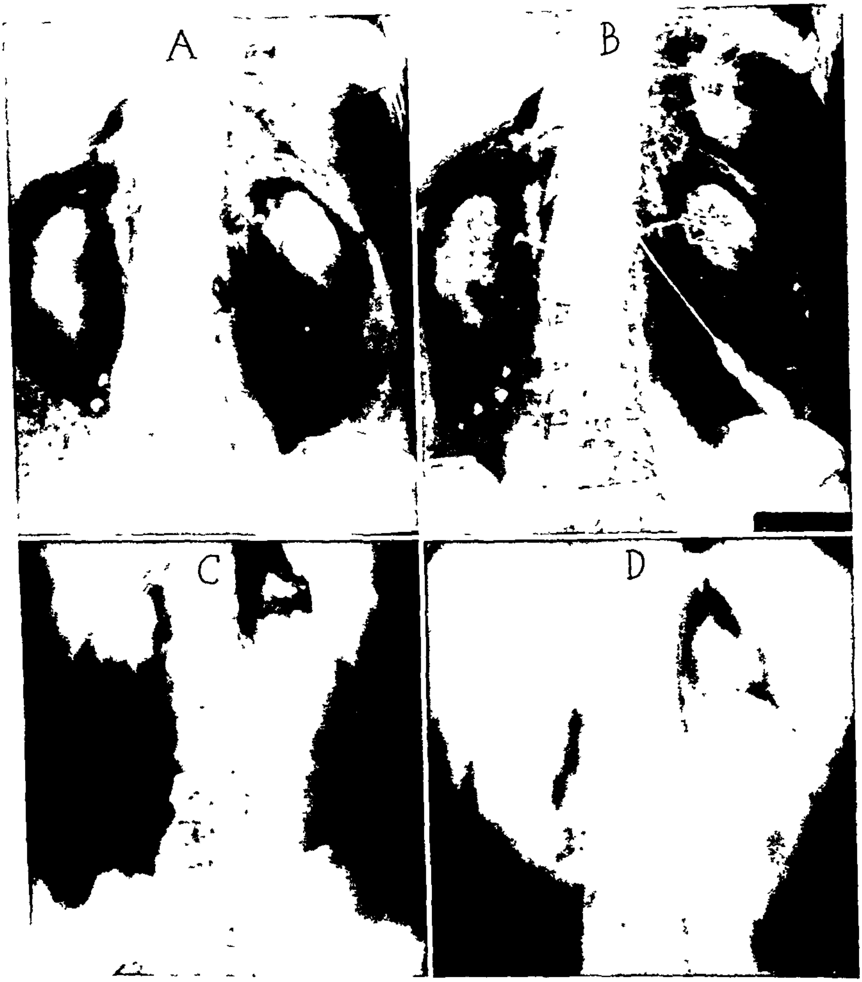

FIG. 2. *A*, perirenal air insufflation of normal case, as seen in *B*. *B*, normal perirenal air insufflation and aortogram Note delineation of renal outline and renal blood vessels as they come to periphery. *C*, paracoccygeal perirenal air insufflation showing normal right adrenal and enlarged left adrenal. Case of benign cortical adenoma. *D*, laminographic study of *C* showing enlarged left adrenal and normal right adrenal gland.

After injection of novocaine, a spinal needle is inserted at the level of the finger tip in the rectum about 1½ inches from the midline and directed anteriorly and medially until the lateral surface of the coccyx is felt. The needle is then directed anteriorly along the side of the coccyx until it rests between rectum and the bone in the midline. In this position, the rectal finger can palpate the

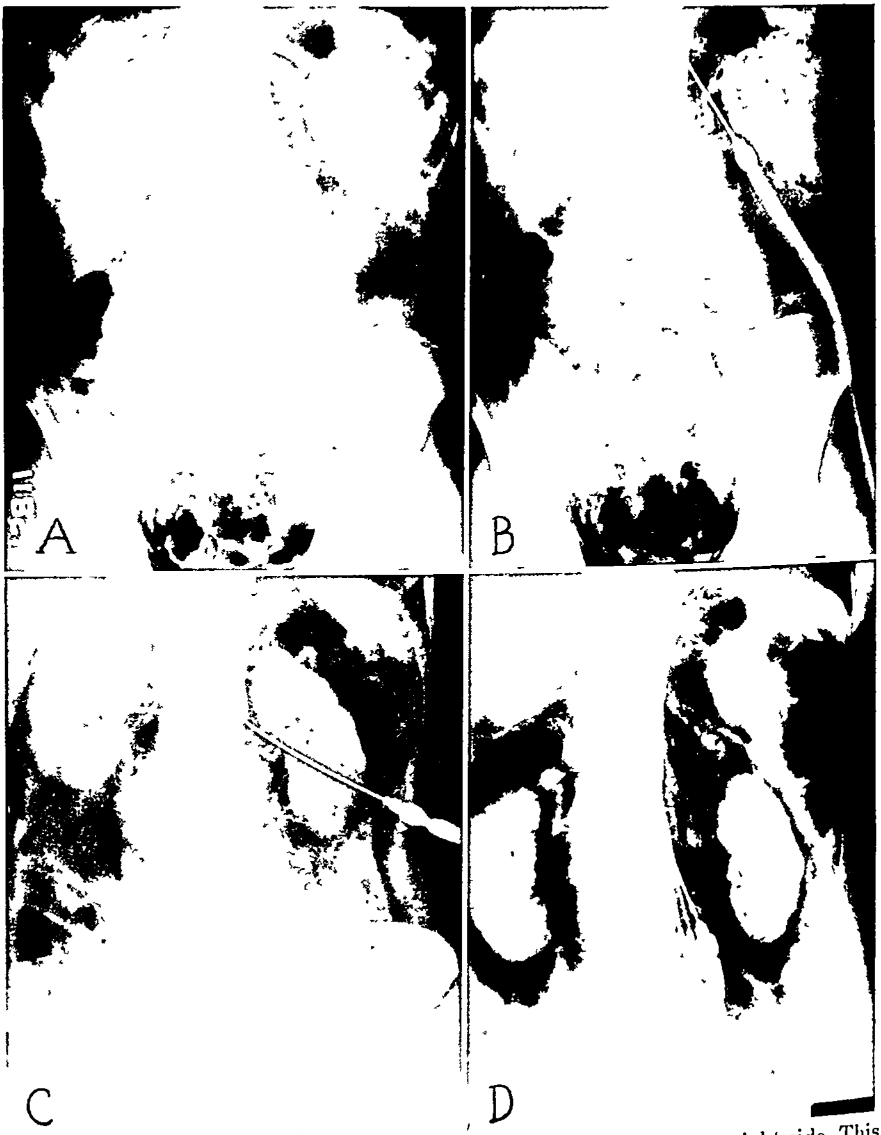

FIG. 3. *A*, perirenal air insufflation of *B*. Note absence of medium on right side. This is typical of distribution encountered when previous surgery or other pathologic processes prevent normal dissection of fascial planes by injected gas. *B*, unknown surgery on right side. Perirenal air insufflation and aortography reveal solitary left kidney. Note absence of right renal artery. Note also hepatic artery on right and splenic artery on left with its branches beyond kidney periphery. *C*, perirenal air insufflation and translumbar aortography revealing intraparenchymal cyst of lower pole of left kidney. Note avascular area in region of cyst, and irregular outline of lower pole of left kidney. *D*, nephrogram effect of *C*.

needle point through the rectal wall during the entire procedure, preventing inadvertent perforation of the rectum. One thousand cubic centimeters of air, oxygen or other gas is injected, the needle is withdrawn and collodion applied to the skin at the site of entrance of the needle. An x-ray is taken immediately to determine the distribution of the medium. Urography and/or translumbar arteriography using 75% neo-iopax may be done in association with this procedure to obtain further data. The following x-rays demonstrate the results of the procedure (figs. 2 and 3).

DISCUSSION

Our series of cases number over two hundred. In only one patient was there a complaint of pain in the left shoulder after introduction of 500 cc of air. The needle was redirected to the right and another 500 cc injected without complaint. X-ray of the chest revealed no abnormality. In an occasional case, there has been mediastinal pressure, neck and scrotal crepitation, without untoward incident.

We believe that paracoccygeal perirenal air insufflation has a definite place in the diagnosis of adrenal, renal, perirenal, retroperitoneal and perivesical disease. It is being used by us in preference to the lumbar approach. It has further advantage in that the demonstration of air about the kidneys is bilateral whereas the lumbar method is unilateral.

This method of accurately and safely directing the passage of the needle by continuous digital palpation through the rectum, in our opinion, insures the proper introduction of the medium. In conjunction with translumbar aortography the perirenal structures as well as the circulation may be visualized and studied in greater detail.

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GASTRO-INTESTINAL MANIFESTATIONS OF URINARY TRACT DISEASE

ALBERT B. KATZ

The importance of digestive tract symptoms in association with diseases of the genito-urinary tract is well recognized. Bockus[1] states that in a series of cases collected by various investigators it is revealed that from 10 per cent to 57 per cent of patients with urinary tract disease have gastro-intestinal symptoms. Important also is the fact that gastro-intestinal symptoms alone were noted in 5 per cent to 38 per cent. Abeshouse[2] states that gastro-intestinal manifestations are by no means an uncommon occurrence in diseases of the upper urinary tract. Practically every case is accompanied by some gastro-intestinal complaint of a transitory or permanent character, i.e., nausea, vomiting, epigastric distress, constipation, or diarrhea. Abdominal surgery, especially appendectomy, was performed in 17 per cent to 37 per cent of cases without relief of symptoms. Since more advances have been made in instrumental diagnostic precision and specialized radiographic technique, fewer errors of this kind have been made.

Abeshouse makes this statement in his treatise: "The importance and necessity of a thorough preoperative urological examination in cases of obscure abdominal pain or uncertain diagnosis is clearly established by the statistical studies of the condition before and after major abdominal operations." Connor[3] reported that 10 per cent of all cases presenting gastro-intestinal symptoms admitted to the Mayo Clinic required urological study. Stevens[4] maintains that urological investigation was indicated in at least one third of all patients entering a hospital with uncertain diagnosis. Statistics from other large clinics reveal that 15 per cent to 20 per cent of patients with renal or ureteral lesions have been previously subjected to abdominal operations for the same complaint. Lowsley and Twinem[5] studied 84 urological cases and noted that 39 patients had previously undergone some major surgical operation without relief of symptoms, and 31 had undergone appendectomy.

Gastro-intestinal factors which are involved in this particular mechanism may be classified as follows: a) toxic; b) neurological or reflex; c) anatomic or mechanical. Any combination of these could cause gastro-intestinal symptoms, as well as each factor individually.

TOXIC FACTORS

Friedenwald and Morrison[6] maintain that in the early stages of the various nephritides the amount of toxic substances accumulating in the blood is slight and, being excreted in small amounts in the gastro-intestinal tract, gives rise

[1] Bockus, H. L.: Gastroenterology, **3:** 990, 1943.
[2] Abeshouse, B. S.: Am. J. Dig. Dis. and Nut., **2:** 477, 1935.
[3] Connor, W. H.: U. S. Navy Bull., **19:** 329, 1920.
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[5] Lowsley, O. S. and Twinem, F. P.: Quoted by Stevens.
[6] Friedenwald, O. O. and Morrison, O. O.: J. A. M. A., **99:** 524, 1932.

to minor digestive disturbances. As the disease process progresses in the renal tract, and the amount of toxic products in the blood increases, these toxic substances are excreted into the gastro-intestinal tract in excessive amounts. This, in turn, gives rise to severe gastro-intestinal ulcerations which result in severe digestive symptoms. The toxic type may be a manifestation of an infectious or uremic process in the renal tract. The occurrence of nausea and vomiting, especially in infection of the upper urinary tract, may be due to bacterial activity and excess nitrogenous retention. It is indicative of failing renal function and is recognized by a high nonprotein nitrogen in the blood.

In acute and chronic forms of nephritis, electrolyte imbalance gives rise to various gastro-intestinal symptoms. Uremia, associated with changes in the carbon dioxide, total base, serum calcium, urea, inorganic phosphates and inorganic acids, affects the gastro-intestinal tract adversely. The vomitus often contains a large amount of urea.

NEUROLOGICAL FACTORS

The "viscero-visceral reflexes" were recognized and described by Mackenzie[7] in 1892. The innervation of the stomach, small intestine, cecum and transverse colon is derived in part from the same source as the kidney and ureter. These alimentary organs receive their nerve supply from the vagus nerve, and the coeliac plexus and its sympathetic branches, and which comes by way of the greater splanchnic nerve from the fifth to the ninth dorsal segments, and through the lesser splanchnic from the tenth to the twelfth dorsal spinal segments. The remainder of the gastro-intestinal canal (descending colon, sigmoid, rectum and rectal sphincter) and the lower genito-urinary tract have a common nerve supply consisting of sympathetic and parasympathetic fibers of the cord. It is, therefore, reasonable to assume that dysfunction of one organ may cause symptoms in other structures which have a similar nerve supply. Hence, pain, nausea, vomiting, belching, epigastric fullness, constipation and diarrhea may result from renal-ureteral lesions. It is because of this reflex mechanism that Smith and Orkin[8] believe that clinically quiescent upper urinary tract lesions give rise to symptoms suggestive of digestive tract disease.

Stimuli originating in the upper urinary tract cause reno-digestive reflexes and also are projected into the various skin zones producing referred pain. Head[9] has studied the topography and mechanism of pain projection on the abdominal wall in renal colic and other renal diseases. The pain is usually associated with localized muscle spasm or rigidity and cutaneous hyperesthesia which may simulate the findings associated with an acute abdominal lesion. The response to stimuli varies in the same or indifferent individuals.

ANATOMICAL FACTORS

The close anatomical relationship of the right kidney and ureter with the duodenum, ascending colon, cecum, liver and gallbladder; and of the left kidney and ureter with the stomach, splenic flexure, descending colon and sigmoid is generally known. Tumors, cysts or abscesses of the kidney may give rise to pain simulating gallbladder disease. Patients with generalized visceroptosis and nephroptosis usually complain of symptoms suggestive of duodenal obstruction due to compression of mesenteric vessels. The effect of drag of the right kidney has been believed to increase duodenal compression.

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[7] Mackenzie, J.: Med. Chron. Manchester, **16:** 293, 1892.
[8] Smith, E. and Orkin, L. A.: Canad. Med. Ass. J., **28:** 281, 1938.
[9] Head, H.: Brain, **16:** 1, 1892.

SYMPTOMS

The types of symptoms are as follows: a) gastro-duodenal; b) biliary; c) appendiceal; d) colonic; 5) peritoneal.

Gastro-duodenal type. The predominant symptoms of this group are nausea, vomiting, epigastric pain, or discomfort, pyrosis and belching, and may be associated with ureteral or renal colic. These symptoms are, in part, compatible with the diagnosis of gastric or duodenal ulcer and such a diagnosis is often made and the usual therapeutic measures are prescribed without success. The occurrence of symptoms of duodenal compression associated with nephroptosis is well known. This results from arterial mesenteric occlusion produced by descent of the kidney producing compression of the duodenum. Bumpus and Thompson in their series of 1,000 cases of ureteral calculi found the pain to be entirely epigastric in 162 cases.

Biliary type. This type is observed only in diseases of the upper urinary tract and is more likely to result from mechanical and pressure effects. Congenital or acquired hydronephrosis, movable kidney, tumors or renal cysts and occasionally renal or ureteral calculi are frequently confused with diseases of the biliary tract. Right upper quadrant pain radiating to the back, nausea, and vomiting are occasionally present when calculi are in the right kidney.

Appendiceal type. Pain in the right lower quadrant is not usually due to acute appendicitis without fever, leukocytosis, pain, rebound tenderness, nausea and vomiting. Diseases of the ureter (stone, stricture) and kidney (stone, hydronephrosis, pyelonephritis) may present symptoms similar to appendiceal disease.

Colonic type. This group of symptoms may be associated with diseases of the urinary tract chiefly with ureteral lesions because of close proximity of the ureter to the colon. The pain is insidious in onset, dull in character and lasts several hours with frequent remissions. Constipation or diarrhea are frequent complaints. Patients with ureteral disease or movable kidney produce tenderness and pain in either the right or left side of the abdomen. Areas of hyperesthesia about the umbilicus may be present. Congenital anomalies of the kidney are frequently accompanied by pain or a sensation of pressure in the abdomen.

Peritoneal type. This group is characterized by a syndrome simulating intestinal obstruction and is not as frequently observed as in other types. Krecke[10] has emphasized the importance of gas retention as a symptom of renal or ureteral disease. These patients complain of upper right abdominal pain or discomfort. These cases are easily mistaken for ileus or appendicitis and are subjected to needless surgery.

[10] Krecke, A.: Munchen. med Wchnschr., **79:** 1556, 1932.

CASE REPORTS

The following are several illustrative case histories:

Biliary type. See figure 1. S. P., a 44 year-old woman, a known hypertensive for many years, complained of right upper quadrant pain radiating to the right side of the back and lumbar region. A history of fat intolerance was present. No urinary symptoms were present. The urine contained a faint trace of albumin at varying intervals. Physical examination was essentially negative except for her blood pressure, which was 192/86. A tentative diagnosis of cholelithiasis was made. A cholecystogram revealed opaque shadows in the region of the gallbladder. A film taken in the erect position showed a normally-filled gallbladder at a lower level, the opaque shadows remaining in the renal area.

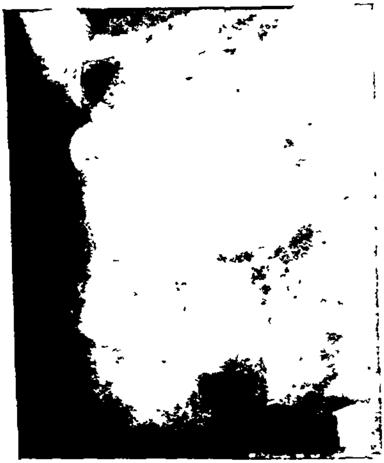

FIG. 1. Cholecystogram reveals calculi within gallbladder. Erect film shows displacement of gallbladder shadow downward with fixation of opaque shadows in renal area.

Because of the hypertension and the opaque shadows in the kidney area, an excretory urogram was done, and the previously reported "gall stone shadows" proved to be within the renal pelvis. Cystoscopy and kidney function tests were done and a nonfunctioning right kidney was found. A right nephrectomy was performed, and a diagnosis of a right calculous pyelonephrosis was made.

The foregoing case indicates the importance of differentiating between renal calculi and cholelithiasis and illustrates the "biliary type" of gastro-intestinal symptoms resulting from the former. The biliary symptoms were due to pressure of a large calculus. It also illustrates the value of careful x-ray procedures, both in the erect and supine positions.

Peritoneal type. See figure 2. K. P., a white woman, aged 42, suffered varying degrees of abdominal distress. Her chief complaint was marked abdominal distention which was partially relieved after belching of gas and passage of flatus. Serial films of the genito-urinary tract made during the course of an excretory urogram showed normal filling of the left renal pelvis, with normal drainage.

On the right side, no dye appeared at any time during the study. The large bowel was considerably distended by gas.

Physical examination had revealed the presence of a large cystic mass occupying the entire right side of the abdomen, which was extremely tender. Blood studies had been normal. Exploratory laparotomy revealed a large cyst of the right kidney which contained about 4,000 cc chocolate-colored urine. The ureter was found to have been tied off at a previous operation. A nephrectomy was performed and the gastro-intestinal symptoms disappeared completely.

The foregoing case illustrates an abdominal syndrome simulating intestinal obstruction or generalized peritonitis and is due to pressure of an enlarged kidney. There are many references in the urological literature to the development of simulated intestinal obstruction or apparent ileus secondary to adjacent pressure. However, the majority of the cases of ileus secondary to disease of the genito-urinary tract have been associated with renal and ureteral calculi. Ileus may also be associated with congenital or acquired hydronephrosis, renal tumors, polycystic disease, renal tuberculosis, pyelonephritis, perinephritic abscess and nephroptosis.

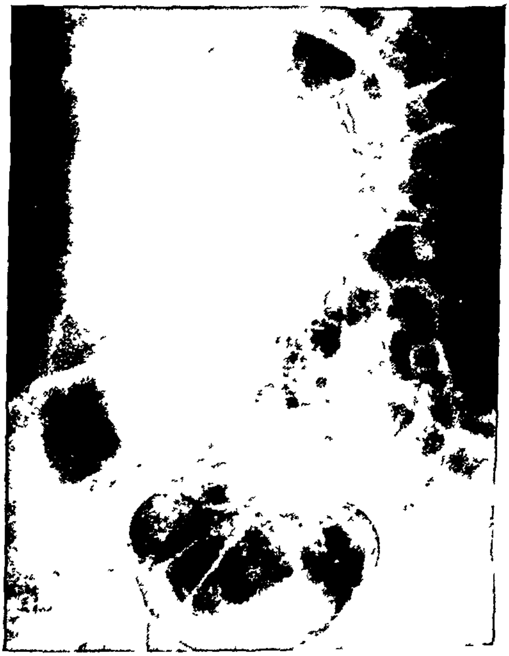

FIG. 2 Normal filling of left renal pelvis with normal drainage. No appearance of dye in right kidney. Large bowel considerably distended by gas.

Colonic type. F. C., a 40 year-old woman, complained chiefly of pain in the left upper quadrant with radiation along the left abdominal wall to the inguinal region. The pain varied in intensity from dull to sharp, had no relationship to the ingestion of food, and was relieved by lying down. She had had frequent attacks of nausea and vomiting, but no urinary symptoms. She had been subjected to an appendectomy and had been treated for an irritable colon for many years. No x-rays of the gastro-intestinal tract or genito-urinary studies had been done previously.

Physical examination revealed tenderness in the left side of the abdomen, and along the left lumbar region. The urine was negative. X-ray examination revealed a normal gastro-intestinal tract. X-rays of the renal tract revealed a large calculus filling the entire pelvis of the left kidney (fig. 3, *A*). A pyelolithotomy was done; the gastro-intestinal symptoms gradually disappeared.

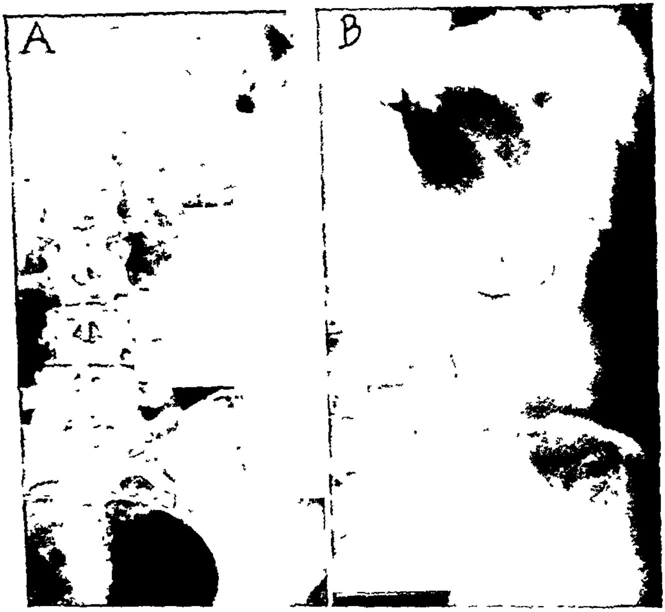

FIG. 3. *A*, flat film reveals large dedritic calculus filling entire pelvis of left kidney. *B*, retrograde pyelogram reveals distortion of renal pelvis and large cystic left kidney.

Another case of the colonic type follows. See figure 3. M. S., a white man aged 53 years, complained of pain in the left upper quadrant, belching, backache, alternating constipation and diarrhea, and weakness for several years' duration. The pain was not related to food or posture. There were no urinary symptoms. He was treated for colitis for several years. Physical examination was negative except for a palpable mass in the left upper quadrant.

X-ray studies of the entire gastro-intestinal tract were negative except for some extrinsic pressure on the splenic flexure. Sigmoidoscopic examination revealed a normal mucous membrane. An excretory urogram revealed a nonfunctioning left kidney and a retrograde pyelogram revealed the presence of a cystic kidney on that side (fig. 3, *B*). A left nephrectomy was performed and all symptoms of colitis disappeared.

The foregoing 2 cases illustrate the fact that various gastro-intestinal manifestations can simultate an irritable colon, and the varied response to the renodigestive reflexes resulted in a mistaken diagnosis.

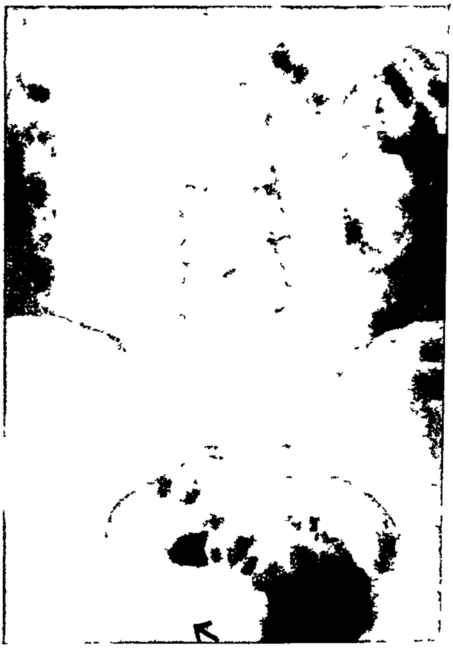

Fig. 4. Excretory urogram reveals small calculus at lower end of right ureter with dilation of ureter above point of obstruction (see arrow).

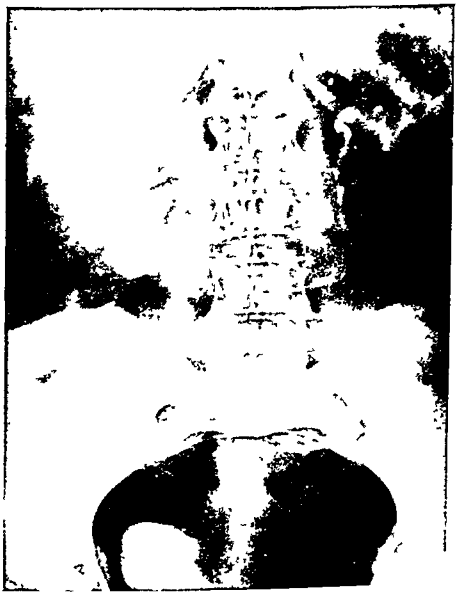

Fig. 5. Excretory urogram reveals ptosis of right kidney with kinking at ureteropelvic junction.

Appendiceal type. See figure 4. A. M., a 36 year-old woman, experienced sudden sharp pain the right lower quadrant accompanied with nausea and vomiting. She had no urinary symptoms, no elevation of temperature and only a slight leukocytosis. An appendectomy was performed that same day and an uneventful recovery was made. Shortly following her discharge, the patient suffered a similar attack of pain, again accompanied with nausea, vomiting and a slight leukocytosis. Studies of the genito-urinary tract revealed a small calculus at the lower end of the right ureter. The ureter was dilated, the stone removed from its location and crushed. The patient's pain disappeared and she has been well since.

The foregoing case illustrates the occurrence of appendiceal symptoms secondary to an impacted calculus in the extreme lower end of the ureter. It is probable that the appendectomy was justified, but this case further accentuates the value of a careful genito-urinary investigation.

Nephroptotic type. See figure 5. B. R., a 38 year-old woman, complained of nausea, vomiting and a dull pain in the right upper quadrant. No x-rays of the gastro-intestinal tract were taken. She had been treated for duodenal ulcer for many years with no relief.

Physical examination revealed a thin, asthenic woman with tenderness over the entire right side of the abdomen. The right kidney was palpable. X-ray studies of the entire gastro-intestinal tract taken later were negative. An excretory urogram revealed a ptosed and rotated right kidney with a kinking of the ureter at the ureteropelvic junction. Proper abdominal support, Trendelenburg position while resting, and a hypernutritious diet was prescribed. The patient's basic symptoms disappeared and a generalized improvement was manifested.

The foregoing case illustrates the gastro-intestinal manifestations associated with a movable kidney and a kinked ureter.

CONCLUSIONS

The gastro-intestinal manifestations of diseases of the upper urinary tract have been classified and the gastro-intestinal manifestations of the reno-digestive reflexes have been discussed.

A complete urological examination is important in every case of obscure abdominal pain and surgery should be postponed until these studies are completed.

Medical Arts Bldg., Philadelphia 2, Pa.

PROGRAM, ANNUAL MEETING, AMERICAN UROLOGICAL ASSOCIATION, HOTEL JEFFERSON, ST. LOUIS, MO MAY 11–14, 1953

MONDAY, MAY 11

Panel Discussion on Pediatric Urology

Moderator	Meredith F Campbell, New York, N Y
Collaborators	Knowlton E Barber, Chicago, Ill Edgar Burns, New Orleans, La Donald A Charnock, Los Angeles, Calif Clyde L Deming, New Haven, Conn

TUESDAY, MAY 12

Persistent Anterior Lobe of Prostate Gland, Oswald S Lowsley, New York, N Y and (by invitation) Alejandro Perez Venero, Panama, Republic of Panama
Discussion Harold P McDonald, Atlanta, Ga

Detection of Early Prostatic and Urinary Tract Cancer in Asymptomatic Patients Fifty Years of Age and Over, Peter J Riaboff, New York, N Y

Bilateral Adrenalectomy for Prostatic Carcinoma, Paul R Leberman and (by invitation) Morton Bogash and Jose Figueroa, Philadelphia, Pa

Intraprostatic Injection of Radioactive Colloids An Experimental Study, Vincent J O'Conor and (by invitation) George J Bulkley and John A D Cooper, Chicago, Ill
Discussion John A Benjamin, Rochester, N Y , J Hartwell Harrison, Boston, Mass , Archie L Dean, New York, N Y , and Frank Hinman, Jr (by invitation), San Francisco, Calif

Furadantin A Study of its Use in Clinical and Laboratory Study, Grayson Carroll, St Louis, Mo
Discussion Edward N Cook, Rochester, Minn , Charles E Friedgood (by invitation) Brooklyn, N Y

The Effect of Antibiotics on Human Spermatozoa, Harry Seneca (by invitation), New York, N Y
Discussion Earl T Engle (by invitation), New York, N Y

Urological Surgery in Combat, Col J E Kimbrough and (by invitation) Lt Col Kryder E Van Buskirk, Washington, D C
Discussion Lt Col David K Worgan, Far East Command

WEDNESDAY, MAY 13

Relative Incidence of Various Pediatric Urological Conditions, John K Lattimer, New York, N Y
Discussion Henry M Weyrauch, San Francisco, Calif , Hugh J Jewett, Baltimore, Md

Urological Anomalies and Complications Associated with Congenital Imperforate Anus, Harry M Spence and (by invitation) H Walton Cochran, Dallas, Texas
Discussion John H Dougherty, Knoxville, Tenn

Some Observations on Cryptorchid Testes, John N. Robinson and (by invitation) Earl T Engle, New York, N Y
Discussion Robert A Moore (by invitation), St Louis, Mo

A NEW CONCEPT OF VESICAL INNERVATION AND ITS CLINICAL APPLICATION, Lowrain E. McCrea, Philadelphia, Pa.
Discussion: S. Richard Muellner, Boston, Mass.

INTESTINOVESICAL FISTULA, George H. Ewell, Madison, Wis.
Discussion: William A. Milner, Albany, N. Y.

RADICAL CYSTECTOMY IN ADVANCED CANCER OF THE BLADDER, Emile S. Sayegh (by invitation), Tanta, Egypt
Discussion: Victor F. Marshall, New York, N. Y.

THE ILIOCECAL SEGMENT AS A SUBSTITUTE BLADDER; a Review of 18 Cases, James W. Merricks and (by invitation), R. K. Gilchrist, Chicago, Ill.
Discussion: Samuel A. Vest, Charlottesville, Va.

PEYRONIE'S DISEASE: A New Approach, Gerald R. Teasley, Texarkana, Arkansas-Texas
Discussion: Miley B. Wesson, San Francisco, Calif.

CARCINOMA OF MALE URETHRA: TREATMENT BY RADICAL PERINEAL EXCISION AND TRANSPLANTATION OF DIVIDED TRIGONE INTO RECTUM, Willard E. Goodwin and Joseph J. Kaufman (by invitation), Los Angeles, Calif.
Discussion: Samuel A. MacDonald, Montreal, Canada

PRESIDENTIAL ADDRESS: MEDICAL EDUCATION AND TRAINING IN UROLOGY, George F. Cahill, New York, N. Y.

THE RAMON GUITERAS LECTURE: RECENT ADVANCES IN EXPERIMENTAL AND CLINICAL CANCER CHEMOTHERAPY, Alfred Gellhorn, New York, N. Y.

THURSDAY, MAY 14

THE INFLUENCE OF DYE BINDING ON EXPERIMENTAL NEPHROCALCINOSIS, Roger Baker, Jerry Reaven and John Sawyer (by invitation), Chicago, Ill.
Discussion: Carl E. Burkland, Sacramento, Calif.

PANEL DISCUSSION ON URINARY LITHIASIS
Moderator: Reed M. Nesbit, Ann Arbor, Mich.
Collaborators: Arthur J. Butt, Pensacola, Fla.
Milo Ellik, Long Beach, Calif.
Rubin H. Flocks, Iowa City, Iowa
Edwin L. Prien, Brookline, Mass.
James T. Priestley, Rochester, Minn.
Howard I. Suby, Boston, Mass.

URETEROVESICAL REFLUX IN PARAPLEGIA (Honorable Mention, Essay Contest), John A. Hutch (by invitation), Vallejo, Calif.

ETIOLOGY, PATHOGENESIS AND DIAGNOSIS OF URETEROCELE, Leonard Paul Wershub (by invitation) and Thomas J. Kirwin, New York, N. Y.
Discussion: Tracy O. Powell, Los Angeles, Calif.

THE INTRAPSOAS TRANSPLANT OF MEGALO-URETER, Hjalmar E. Carlson, Kansas City, Mo.
Discussion: Samuel N. Vose, Boston, Mass.; Carl Rusche, Hollywood, Calif.

A PELVIC FLAP OPERATION FOR CERTAIN TYPES OF URETEROPELVIC OBSTRUCTION: OBSERVATIONS AFTER TWO YEARS' EXPERIENCE, Ormond S. Culp and (by invitation) James F. DeWeerd, Rochester, Minn.
Discussion: Frederic E. B. Foley, St. Paul, Minn.; Robert B. McIver, Jacksonville, Fla.

THE VENOUS JUNCTION OF THE GLOMERULAR ARTERY, Armando Trabucco and (by invitation) Fernando Marquez, Buenos Aires, Argentina
Discussion. William Wallace Scott, Baltimore, Md.

CLINICAL APPLICATION OF BLOOD VOLUME STUDIES IN MAJOR SURGERY, Charles Barbour and Robert Tennant (by invitation), Hartford, Conn
Discussion· Donald C Malcolm (by invitation), Los Angeles, Calif

HISTOPATHOLOGY IN PROGNOSIS OF KIDNEY TUMORS, William A Barrett and Edward J. McCague, Pittsburgh, Pa
Discussion: Hugh T. Beacham, New Orleans, La

PHEOCHROMOCYTOMA A CLINICO-PATHOLOGICAL ANALYSIS OF 23 CASES, Meyer M Melicow (by invitation), New York, N. Y
Discussion. James H. Semans, Atlanta, Ga

SCIENTIFIC EXHIBITS*

Influence of Prostatic Cortex in Transurethral Resection, Milton A. Antipa and Ranulf P. Beames (by invitation), San Francisco, Calif.

Blood Volume Determinations as a Guide to Intravenous Therapy: Experiences of a General Hospital, Charles M. Barbour and Robert Tennant (by invitation), Hartford, Conn.

Leonardo da Vinci's Studies of the Genito-Urinary System, Elmer Belt and (by invitation) Kate Trauman Steinitz and Wilfred Haflinger, Los Angeles, Calif.

Regeneration of the Urinary Bladder in the Dog, A Waite Bohne (by invitation), Detroit, Mich.

Nephrotomograph, Mitchell Price, William Dubilier, Jr., John A. Evans and James C. Monteith (by invitation), New York, N. Y.

Tissue Culture in Urology, R. G. Bunge, Iowa City, Iowa

The Intrapsoas Transplant of Megalo-Ureter, Hjalmar E. Carlson, Kansas City, Mo.

A Pelvic Flap Operation for Certain Types of Ureteropelvic Obstruction, Ormond S. Culp, Rochester, Minn.

Photographic History of the American Urological Association, Wirt B. Dakin, Los Angeles, Calif.

Evolution of the Evacuator, Milo Ellik, Long Beach, Calif.

Use of the Polaroid Land Camera in Urology, Manley L. Ford (by invitation) and Walter A. Keitzer, Akron, O.

Technique of Open Transcolonic Ureterosigmoidostomy, Willard E. Goodwin and Mary P. Goodwin (by invitation), Los Angeles, Calif.

Furadantin in Urinary Infections, Howard B. Hasen (by invitation) and Thomas D. Moore, Memphis, Tenn.

Medical Adrenalectomy in Prostatic Cancer, Frank Hinman, Jr. and Gerald M. Miller (by invitation), San Francisco, Calif.

Clinical Application of the Skeggs-Leonards Artificial Kidney, Walter A. Keitzer, Akron, O.

Carcinoma of the Prostate, Col. J. C. Kimbrough and (by invitation) Major F. E. Cox, Lt. Col. Kryder VanBuskirk, and Capt. Anthony Borski, Washington, D. C.

Unusual New Operations, Oswald S. Lowsley, New York, N. Y.

Clinical and Experimental Uses of 70 Per Cent Urokon in Urology, William F. Melick and (by invitation) Joseph J. Naryka and John E. Bryne, St. Louis, Mo.

Criteria for Pathological Diagnosis of Carcinoma of Prostate, F. K. Mostofi, Washington, D. C.

Furadantin in Genito-Urinary Infections, Charles M. Norfleet, Jr. (by invitation), Fred K. Garvey and (by invitation) William H. Boyce, Winston-Salem, N. C.

Newer Diagnostic Methods in Urology, Samuel H. Rothfeld, Manhasset, N. Y., Frank C. Hamm, Harrison C. Harlin and (by invitation) Miles W. Thomley, Brooklyn, N. Y.

Theory and Treatment of Physiological Tumors of the Urinary Tract, Lt. Col. Richard W. Satterthwaite, Waltham, Mass.

Urine and the Ground Substance, Joseph Seifter (by invitation), Arthur J. Butt and (by invitation) Ernst A. Hauser, Pensacola, Fla.

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*The Scientific Exhibit has been erected under the supervision of the Director of Exhibits, Mr. William P. Didusch.

TECHNICAL EXHIBITS

Mr. William P. Didusch, *Director*

NAME AND ADDRESS OF FIRM	BOOTH NUMBER
American Cystoscope Makers, Inc , New York	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12
Ayerst, McKenna and Harrison, Ltd , New York, N. Y.	29
C. R Bard, Inc., Summit, N. J.	20, 21, 22, 23
Birtcher Corporation, Los Angeles, Calif.	31, 32
Ciba Pharmaceutical Products, Inc , Summit, N. J.	38
Coca Cola Co., Atlanta, Ga. ..	36
Eaton Laboratories. Inc., Norwich, N. Y.	33
Liebel, Flarsheim Co., Cincinnati, O.	26, 27
J. B. Lippincott Co , Philadelphia, Pa	15
P. Lorillard Co , New York, N. Y.	46
Mallinckrodt Chemical Works, St. Louis, Mo.	42, 43
Merck & Co Inc , New York, N. Y.	40
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Philip Morris & Co. Ltd , New York, N. Y.	44
V. Mueller & Co , Chicago, Ill.	17, 18
National Electric Instrument Co Inc , Elmhurst, N Y	45
Nepera Chemical Co. Inc , Yonkers, N Y.	41
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BILATERAL GIANT HYDRONEPHROSIS

DAVID M. DAVIS

On October 7, 1946 there was admitted to the medical service of the Jefferson Hospital a man with an enormously swollen abdomen. He was in a semistuporous condition, and the admitting house officer assumed at once that he was dealing with a case of ascites, probably due to cirrhosis of the liver.

On the medical ward it was observed that there was also edema of the legs, difficulty and frequency of urination, blood urea nitrogen of 50 mg. per cent, and blood creatinine of 4.3 mg. per cent. Alerted by these findings, the medical service began a thorough investigation. The wisdom of this step is shown by the ultimate result. Immediate paracentesis might have had serious consequences.

Eventually a fairly accurate history was obtained. The patient was a welder, aged 43. His health had been good until about 2 years previously, when he noticed blood in the urine. This hematuria was unaccompanied by any other symptoms. There were several such episodes, all treated by bed rest and oral medication, and all of short duration. In January 1946, ten months before admission, enlargement of the abdomen was first noted, and frequency of urination, both diurnal and nocturnal, began. The abdominal enlargement progressed steadily, and there were added constipation, nausea and vomiting. As so often happens, one wonders why the symptoms were allowed to become so severe before the patient found his way to the hospital.

On physical examination, the abdominal swelling was found to be compressible and gave the impression of being due to a collection of fluid under tension. The urine was clear and uninfected, but did contain a trace of albumin. Phenolsulfonphthalein given intravenously was not excreted at all in one hour. The prothrombin time was 50 per cent of normal.

A barium enema showed a huge mass, obviously arising centrally in the posterior part of the abdomen, pressing the colon out peripherally in all directions and pushing away the small intestines (fig. 1, *A*). All of this made the urinary tract suspect, so that cystoscopic examination was clearly indicated.

With the panendoscope moderate prostatic hypertrophy was seen, with a hypertrophic bar, causing definite obstruction as evidenced by muscular hypertrophy of the detrusor muscle and of the trigone and ureteral ridges. Catheters passed easily up the ureters, apparently reaching both kidneys. From the right kidney 350 cc of clear urine was aspirated, but from the left catheter nothing came. Accordingly a moderate quantity of skiodan solution was injected in both catheters, and a film taken.

The plain film taken before the injection showed the right catheter following a normal course, but the left one was deflected sharply to the right so that its upper extremity lay about over the right anterior superior spine of the ileum (fig. 1, *B*). After the injection, one could see a large right hydronephrosis, but on the left side only the ureter was filled. The right ureter appeared about normal, indicat-

Accepted for publication May 27, 1952.

ing that the obstruction producing the right hydronephrosis was at the ureteropelvic junction (fig. 1, *C*). It was reasonable to assume, therefore, that a more pronounced ureteropelvic obstruction was present on the left side, and that the great swelling of the abdomen represented a huge hydronephrosis. The author thought that the left kidney probably was a pelvic ectopic kidney, on the ground that a displacement of the ureteropelvic junction from its normal position in the left upper abdomen to a point overlying the right anterior superior spine of the ileum was scarcely conceivable. It was however recognized by all that the tumor might be a solid one, and that no certain diagnosis could be made. The problem was intensely interesting to everyone concerned, and the discussion was keen and extensive. The two points clear to all were that exploration was necessary to ascertain the facts regarding the great mass and the state of the left kidney, and that right nephrostomy for drainage should be carried out as soon as possible.

On October 16, 1946 exploratory operation was performed by Dr. Baker. Incision was made in the left lower quadrant, and the peritoneum was pushed away from the mass. It became obvious that the mass was cystic, so that a small incision was made in it and a large dePezzer drain was inserted. Through this tube clear fluid to the amount of 8½ litres was drained off. This appeared to show that the mass was actually a hydronephrosis, and an x-ray film made in a few days after injecting 1500 cc of skiodan solution through the drainage tube fully established the diagnosis (fig. 1, *D*). In viewing this roentgenogram one should not forget that the injected opaque medium was little more than one-sixth of the amount of the original contents of the hydronephrosis.

The patient's general condition improved at once after the left nephrostomy, so that on November 6, 1946, right nephrostomy was carried out, releasing this time between 300 and 350 cc of clear fluid which was definitely urinous. Urine continued to drain in large quantities from the right side, but the drainage from the left side was never abundant, and soon became mucopurulent. Nevertheless the patient's improvement continued rapidly, and on December 24, 1946, eleven weeks after admission, he was discharged with the two drainage tubes in place and feeling very well indeed. The phenolsulfonphthalein excretion from the right kidney had gone as high as 20 per cent in one-half hour.

On March 1, 1947 the patient was re-admitted to the hospital. He complained of anorexia, fatigue and general malaise. The blood urea nitrogen was 20 mg. per cent and the phenolsulfonphthalein excretion from the right kidney only 10 per cent in one-half hour. There was never any phenolsulfonphthalein excretion from the left kidney. As soon as the tubes were properly serviced and good drainage re-established, the patient's well-being was restored and the phenolsulfonphthalein excretion from the right kidney rose to 30 per cent in one-half hour. On March 11, 1947 the left kidney was removed by Dr. Emanuel Lubin, at that time Reisdent in Urology at the Jefferson Hospital. It stripped away from the peritoneum fairly easily, and proved to be a mere shell less than one millimeter thick everywhere except for a few small masses of solid tissue, none more than 10 millimeters thick. The pedicle sprang from its usual location, showing that this

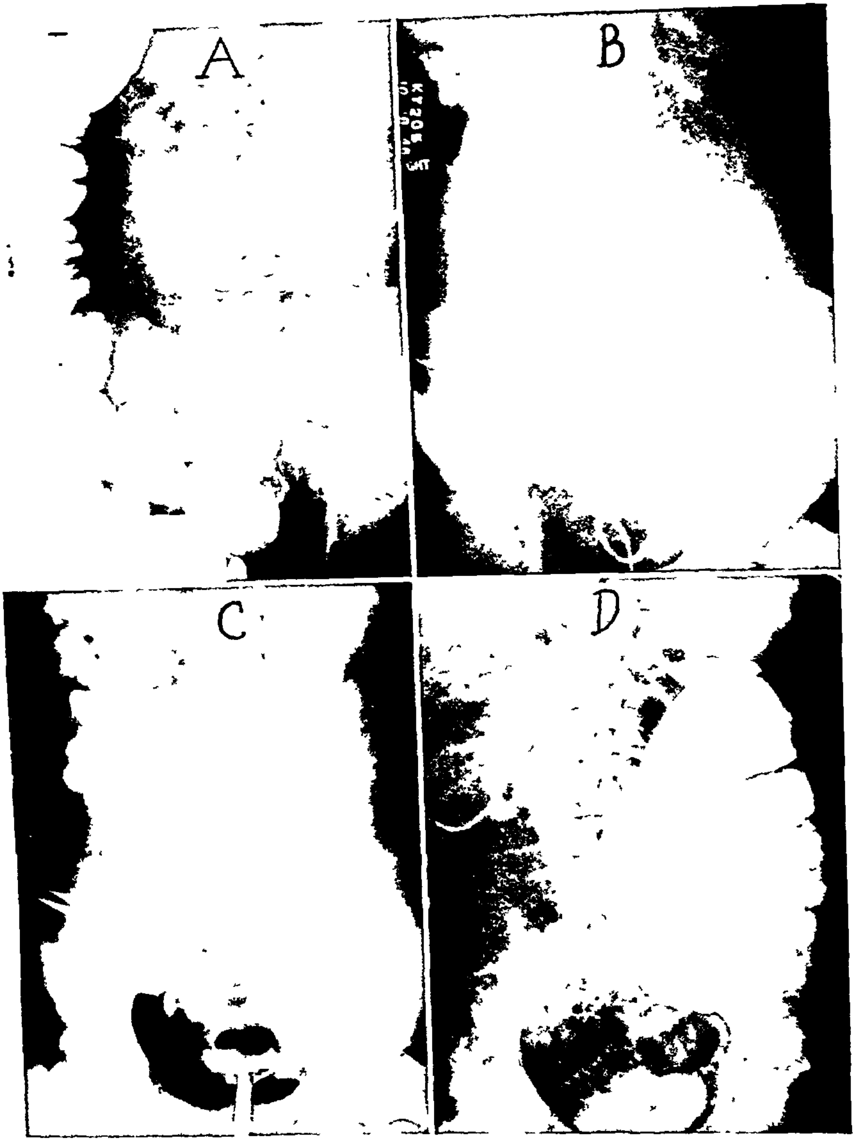

FIG. 1. *A*, barium enema. Note very small amount of intestinal gas. *B*, two catheters in left ureter. Note that the tip of the longer catheter lies close to the right anterior superior spine of the ilium. *C*, right retrograde pyelo-ureterogram, left retrograde ureterogram. Apparently no skiodan has entered the left pelvis. *D*, left antegrade pyelogram made after bilateral nephrostomy. Note change of position of left ureter, showing how much left pelvis has shrunk.

kidney had originally occupied a normal position, and was not a pelvic ectopic kidney. The ureteropelvic junction was very small, barely admitting a 2 mm. probe under firm pressure. The patient recovered quickly and was discharged on March 26, 1947.

In the early part of May 1947, the right nephrostomy tube accidentally came out, and chills and fever quickly followed. There was a short hospital stay, during which the tube was replaced and antibiotics were given. At the time of discharge on May 25, 1947 the phenosulfonphthalein excretion was 25 per cent in one-half hour, and the blood urea nitrogen was 9.8 mg. per cent.

The improvement had now reached such a point that the possibility of relieving the right ureteropelvic obstruction and restoring the right ureter to function was seriously considered. X-rays taken after injecting opaque medium through the drainage tube showed the location of the obstruction very clearly (fig. 2, *A*). Accordingly the patient was admitted to the hospital for the fourth time on November 7, 1947, and on November 14 right intubated ureterotomy was performed by the author. The very small, stenosed ureteropelvic junction was incised in the direction of the long axis of the ureter, the incision was continued down the ureter to a point where it became of normal size, and the ureter was intubated with a 14F tube (4⅔ mm. in diameter). This splinting tube remained in place 4 weeks. After its removal x-ray films showed that opaque solution injected through the nephrostomy tube passed easily and quickly down the ureter to the bladder (fig. 2, *B*). The nephrostomy tube was therefore clamped. There was no leakage about it, the patient suffered no discomfort, and his temperature remained normal. The blood urea nitrogen remained at 14 mg. per cent and the phenolsulfonphthalein excretion at 30 per cent in one-half hour.

During this admission transurethral prostatic resection was carried out. The patient was sent home on December 20, 1947 with the nephrostomy tube still in place, but permanently closed by a screw clamp. This arrangement worked so well that the final removal of the nephrostomy tube was put off repeatedly and for a long time.

In October 1948, two years after the original admission, the situation was reviewed in the hospital. The right kidney was secreting from 1000 to 1500 cc of clear urine each 24 hours. The renal pelvis accepted 250 cc of opaque medium, and roentgenograms showed that the ureter emptied it completely in 1½ hours. Cystoscopy showed that the transurethral prostatic resection had been incomplete, some obstruction remaining. A No. 14 bulb passed up the right ureter to the kidney easily. The general situation was such that the idea of removing the tube was shelved, and, as it turned out, not seriously taken up again for over two years.

Another study in the hospital, in February 1950, showed the kidney urine to be alkaline, with a pH of 8.0, and infected with cocci and bacilli. Continuous irrigation with Suby's solution was given, bringing the urine to an acid reaction, but not eradicating all bacteria. The right ureter accepted a No. 12 bulb easily. In spite of all this, the phenolsulfonphthalein excretion reached 35 per cent in one-half hour.

In January 1951, we decided to make a final determined effort to get rid of the nephrostomy tube and restore the patient to full activity. His general condition was good but the presence of the tube encouraged him to think of himself as an invalid. There was some frequency and burning on urination, so that the remaining bladder neck obstruction was removed by a second transurethral resection performed February 1, 1951 by Dr. Joseph Wilkerson. This was so successful that before he left the hospital he was able to void into the uroflowmeter 600 cc of urine at a rate of 50 cc per second (22 cc per second is considered to be the lower limit of normal).

The expulsive force and emptying power of the renal pelvis were measured by attaching a vertical glass tube to the nephrostomy drainage tube. It was observed that the pressure in the tube had to be raised to 22 cm. (of water) before fluid began to enter the pelvis, but that if nothing was injected the urine would rise in the vertical tube to a point 15 cm. above the level of the kidney, after which all urine secreted would pass down the ureter to the bladder. This, of course, is a higher pressure than is supposed to be normal for the renal pelvis, but it caused no pain, fever, or other untoward manifestations, and was thought to be the best obtainable under the circumstances. It is to be hoped that further similar observations in the future will increase our knowledge on this subject. Residual urine in the pelvis was determined by opening the nephrostomy tube each morning after it had been clamped all night. No more than 25 cc was ever found in it. The phenolsulfonphthalein test showed 37 per cent excretion in one-half hour and the blood urea nitrogen level was 14 mg. per cent. In view of all these favorable findings it was at last thought permissible to remove the nephrostomy tube.

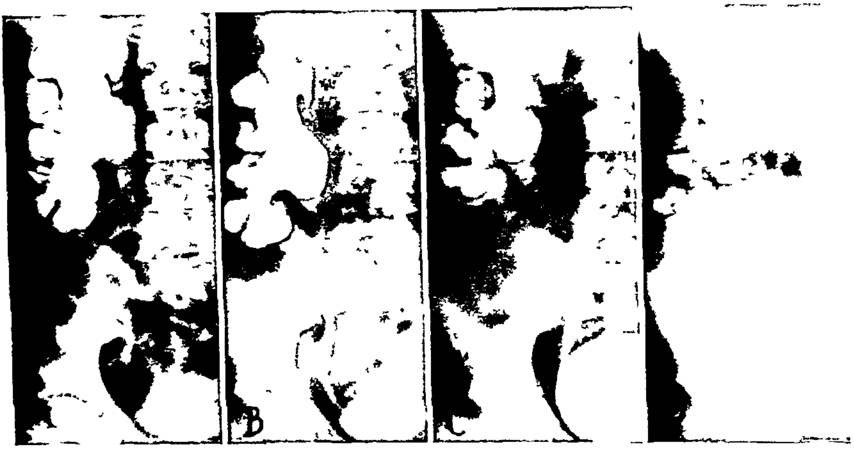

FIG 2 *A*, antegrade right pyelogram before operation on ureteropelvic junction. Note absence of skiodan in ureter, indicating ureteropelvic obstruction *B*, antegrade right pyelogram after intubated ureterotomy. Note excellent flow of opaque medium in ureter and bladder *C*, excretory urogram (20 minute film) after removal of nephrostomy tube. *D*, same, 1¼ hour film, showing fairly good emptying

It was finally removed February 25, 1951, four years and 3 months after it had been inserted. Urine drained through its tract for a few hours only, and the patient felt no ill effects of any kind. Excretory urography showed the right kidney still, of course, markedly hydronephrotic, but very much less so than at the beginning. At the end of an hour and a quarter the caliber of the infundibula was definitely lessened, and most of the opaque medium (urokon) had left the kidney. Phenolsulfonphthalein excretion and blood urea nitrogen remained at normal levels. The patient left the hospital March 16, 1951.

At the present time he feels himself to be in perfect health and is back at work as a welder at the Philadelphia Navy Yard. Renal functional tests remain at normal figures, and the voiding function is normal, with no nocturia.

It seems to us that this case demonstrates quite clearly a number of propositions, as follows:

First, congenital ureteropelvic stenoses, severe enough to cause marked hydronephrosis, can exist for many years without symptoms.

Second, the recuperative powers of hydronephrotic kidneys, once the obstruction is thoroughly relieved, are very great and at times really spectacular.

Third, obstructive lesions must be sought for throughout the entire extent of the urinary tract, and, if more than one be present, every one must be completely relieved in order to obtain the best results.

Fourth, nephrostomy drainage is not only a life-saving procedure, but may be maintained over long periods of time to protect the kidney from damage while multiple obstructive lesions are being corrected.

Fifth, intubated ureterotomy is a satisfactory procedure for the relief of ureteropelvic obstruction, and

Sixth, the renal parenchyma and pelvis and the ureter can and will function satisfactorily in the presence of an intrapelvic pressure as high as 15 cm. of water.

It is to be hoped that more studies comparable with this will be carried out, and that they will lead to a better knowledge of what constitutes the normal ntrapelvic pressure.

255 S. 17th St., Philadelphia 3, Pa.

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STREPTOMYCIN, PAS AND ISONIAZID IN RENAL TUBERCULOSIS

JOHN K. LATTIMER, FRED LERMAN, PHILIP LERMAN AND LOUIS L. SPIVACK

From the Squier Urological Clinic, Columbia University College of Physicians and Surgeons, and the Research Unit for Genito-Urinary Tuberculosis, Kingsbridge Veterans Hospital, Bronx, New York 68, N. Y.

Four hundred fifty-eight cases of genito-urinary tuberculosis have been treated with chemotherapy alone by the Research Group of the Veterans Administration, Army and Navy. The objective of this group has been to determine the optimum long-range dosage plan for streptomycin and other new anti-tuberculosis drugs. This study is now 5 years old. Symptomatic, roentgen, and bacteriological evidences of benefit from chemotherapy have been observed.

Symptomatic improvement has been impressive. About 50 per cent of our patients with renal tuberculosis had frequency or dysuria at the beginning of treatment. Among these, the majority registered marked improvement. With the healing of bladder ulcers, these men were relieved of their severe pain, and were again able to sleep at night. Many patients who had been economic cripples have now returned to work. Improvement was noted even in patients where the urine remained positive for tubercle bacilli. The dull kidney pain, frequently found with renal tuberculosis, was not improved, however.

Roentgen evidence of benefit from chemotherapy was more difficult to assess. The progress of tuberculous cavitation appeared to halt, in both small lesions (fig. 1) and in massive lesions, when judged by serial pyelograms. Strictures of calyceal necks, or of ureters, sometimes contracted rapidly during treatment, however. This led to a policy of excretory urograms every 4 months during treatment. Thus, if ureteral strictures were discovered early, they could be successfully dilated, and usually stayed open thereafter.

BACTERIOLOGICAL RESULTS

Treatment was judged successful only if the tubercle bacilli disappeared from the urine by culture. This was a most demanding criterion. Patients who had active lesions in the kidneys and in the genitalia, at the same time, were the most difficult to convert to negative urines. Those with kidney lesions only, were less difficult, and those with prostatic lesions alone were the easiest to convert.

COMBINED INTERMITTENT TREATMENT

Combined therapy (streptomycin 1 gm. every third day, plus PAS 12 gm. daily) appeared to be superior to streptomycin alone (fig. 2). It did not appear necessary to give streptomycin daily; toxicity was less and patient tolerance much

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Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinions or policy of the Veterans Administration

Read at annual meeting, American Urological Association, Atlantic City, N. J., June 22, 1952

The isoniazid used in this study was generously provided by the E. R. Squibb and Sons of New York in the form of their product, Nydrazid.

greater when streptomycin was given intermittently, every third day. Duration of treatment has been lengthened to a period of at least one year, in view of the fact that the combined intermittent treatment greatly defers the development of drug resistance. If pyuria was present at the end of one year, the treatment was continued for two or even three years.

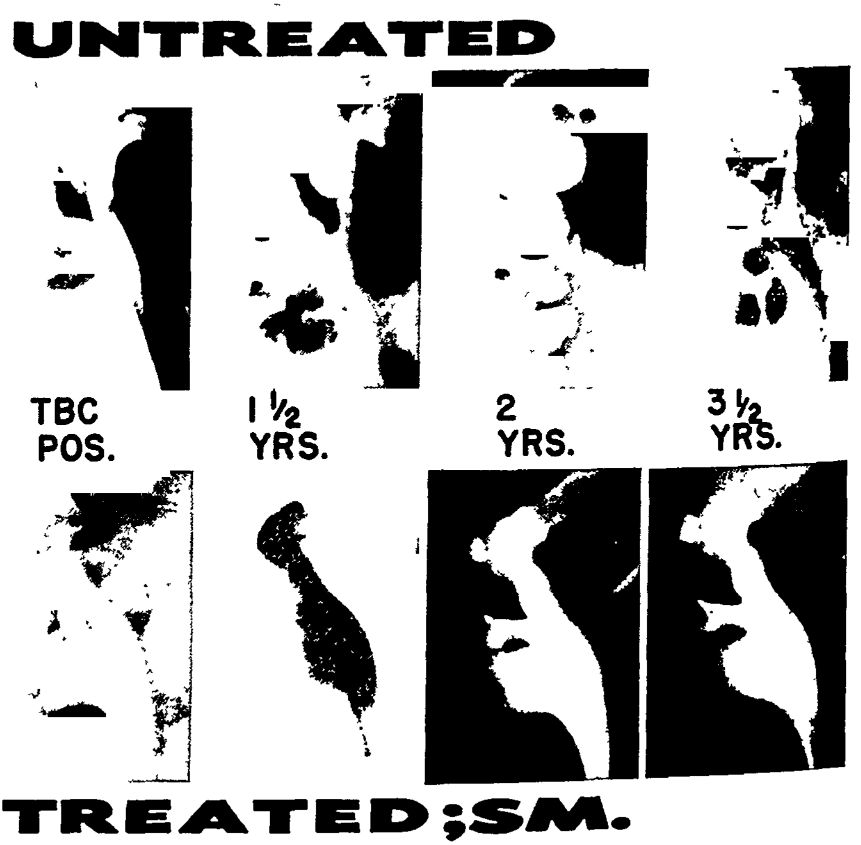

FIG. 1. Both upper and lower kidneys started with small tuberculous lesions. Untreated kidney (top) became so badly damaged after 3½ years, that it was unable to support life. Treated kidney (bottom) became negative by culture, however, and stopped disintegrating.

SIZE OF RENAL LESION VS. PROGNOSIS

The larger the renal lesion, the worse the prognosis. Kidneys with *massive renal lesions* could not be permanently converted with streptomycin and PAS. Several of these patients converted for periods of from 1 to 2 years but none of these lesions has remained negative for 5 years. *Medium-sized lesions,* where only one calyx was involved, showed 20 per cent conversions after 5 years. Many of these patients are now back at their normal occupations. One of these men was negative for 4 years before relapsing and becoming positive again. His cavitary lesion was then removed by partial nephrectomy (fig. 4). *Small renal lesions* responded well to treatment with streptomycin and PAS. Eighty per cent of

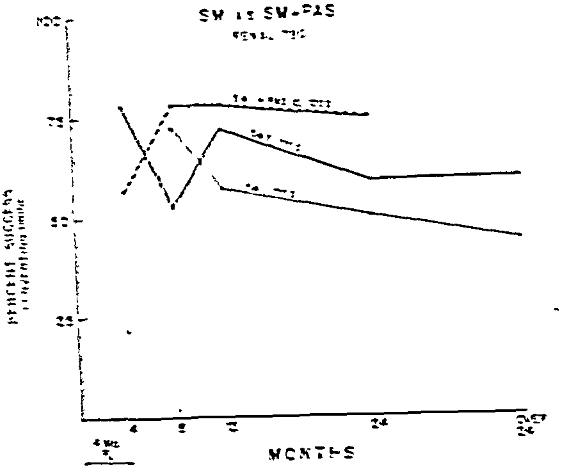

FIG. 2. Combined treatment with streptomycin plus PAS (top line) was superior to streptomycin alone (even the 2 gm. dose). Conversion rates were higher, and toxicity was less with combined treatment. Development of drug-resistance was also deferred by combined regimen. At least 1 year of combined treatment is now advised.

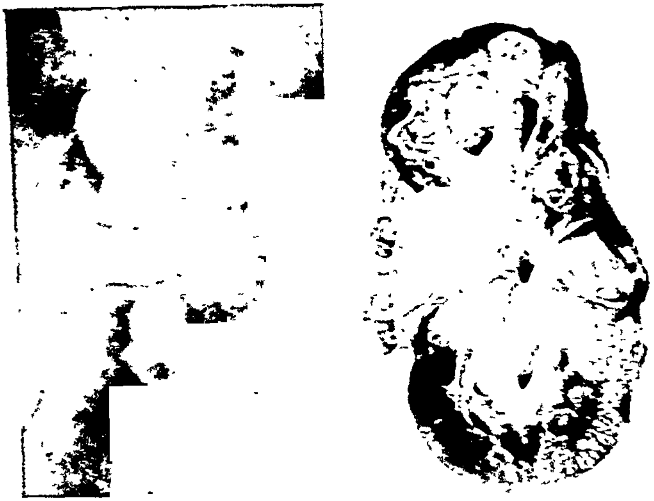

FIG. 3. Very large lesions, of this type, with moth-eaten calyces, strictures and cavities could not be permanently converted. Most of parenchyma of this kidney is reduced to fibrocaseous scar tissue. Very small renal lesions, on other hand, where no deformity of pyelogram had been produced, gave very good 5-year conversion rates.

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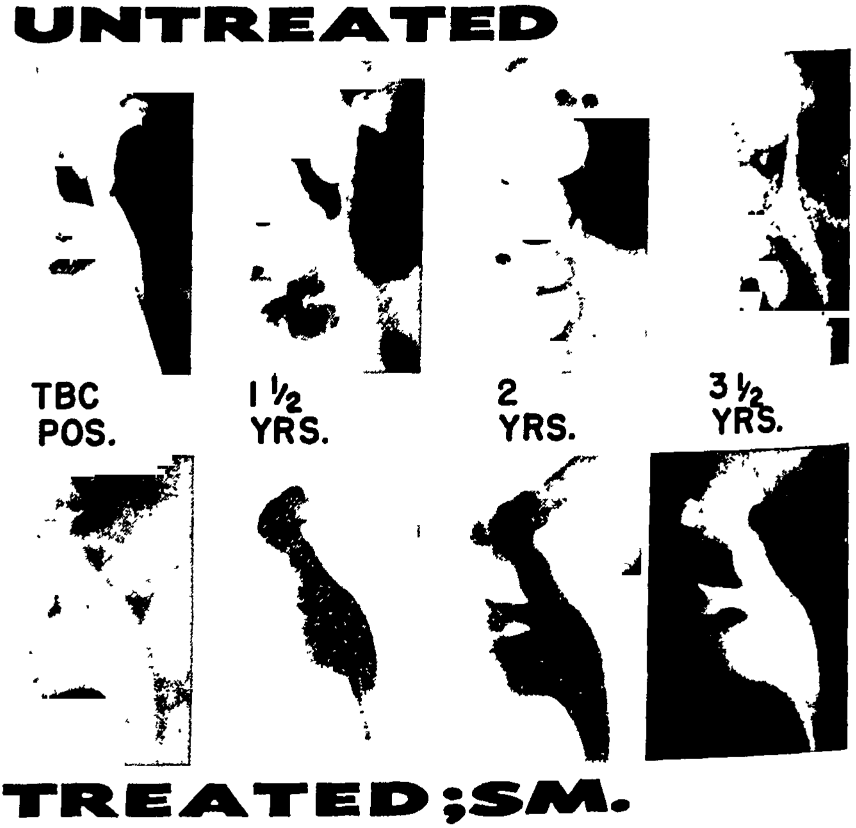
It was concluded that "any lesion large enough to be definitely visible in a pyelogram" was very difficult to convert to negative urine. Unfortunately, patients with "small" renal lesions are almost never seen by the practicing urologist.

greater when streptomycin was given intermittently, every third day. Duration of treatment has been lengthened to a period of at least one year, in view of the fact that the combined intermittent treatment greatly defers the development of drug resistance. If pyuria was present at the end of one year, the treatment was continued for two or even three years.



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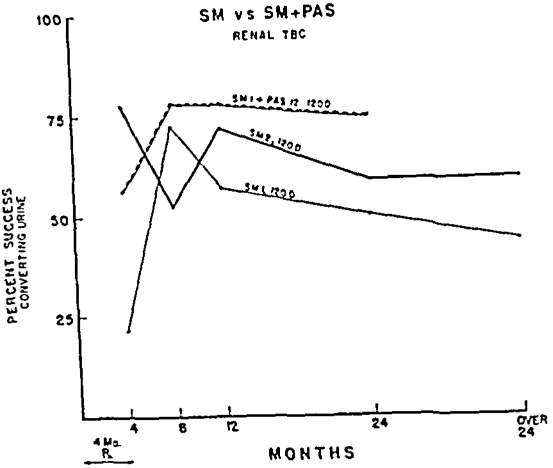

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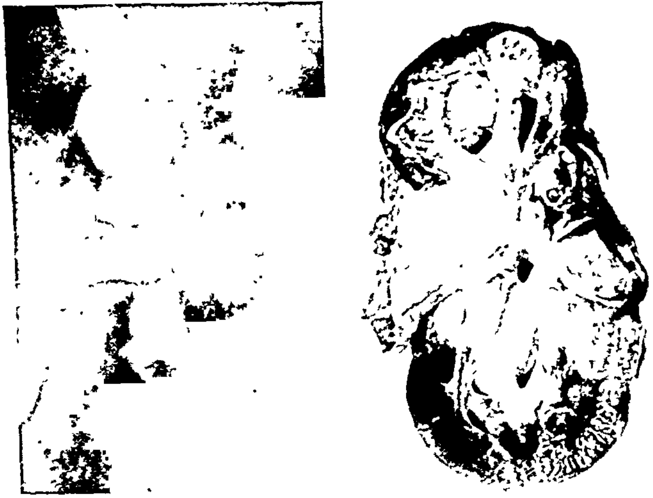

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These patients may not develop urinary symptoms for several years. They may be discovered only by the surgeon who removes a tuberculous kidney and then watches the other "good" kidney for the first sign of breakdown in the form of pus cells or tubercle bacilli in the ureteral urine. They may also be found by medical men or orthopedists who specialize in pulmonary or bone tuberculosis, who watch their patients for pus cells, albumin or tubercle bacilli in the urine as part of the routine checkup. A periodic urine analysis should certainly be done on every patient who has tuberculosis in any part of the body.

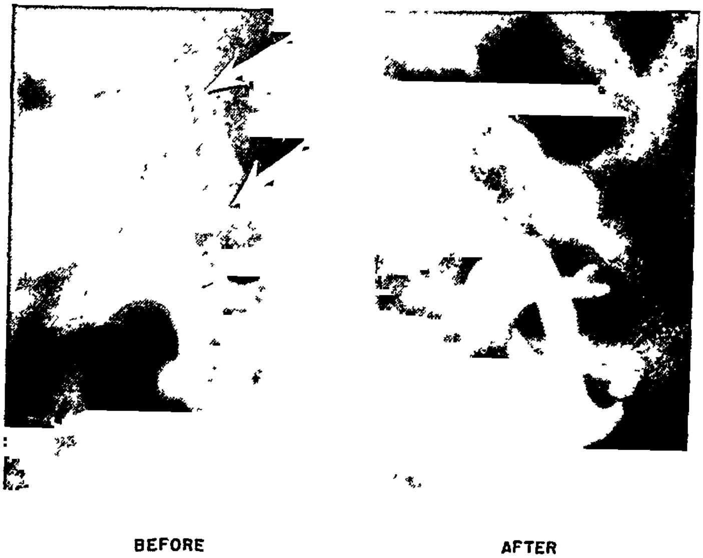

FIG. 4. In occasional cases where tuberculosis was confined to only one portion of kidney, (arrows), partial nephrectomy was possible. These operations were preceded by and "covered" with massive chemotherapy.

SURVIVAL

In one group of 278 patients, only two have died of uremia. There were 13 other deaths in this group, which were due to pulmonary tuberculosis, but without uremia. Considering the fact that many of the patients treated had massive tuberculous involvement of their solitary kidney, this survival rate is impressive, and is probably better than would have been expected had no chemotherapy been given.

GENITAL TUBERCULOSIS

Most cases of genital tuberculosis in this series appeared to result from contamination of the prostate by the infected urine from tuberculous kidneys. In patients where the urine was positive for tubercle bacilli because of a prostatic focus, the immediate results appeared to be good. In some cases, however, a large tuberculous nodule on the prostate eventually broke down again and began to discharge tubercle bacilli. These nodules did not decrease in size after streptomycin treatment. In rare cases which did persist, causing the urine to be positive despite chemotherapy, total prostatovesiculectomy was advised, under cover of PAS and streptomycin. All tuberculous nodules in the epididymis were removed as soon after diagnosis as the patient's general condition would permit. All operations on the genito-urinary tract were "covered" by streptomycin and PAS for three weeks, or until pyuria ceased. This sometimes required many months of treatment.

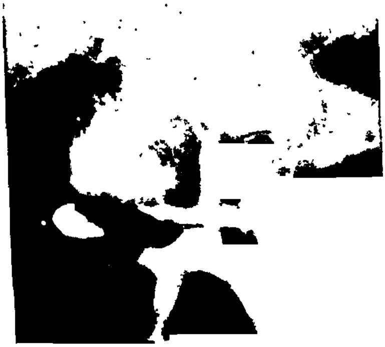

FIG. 5. Massive renal lesions of this type contained enough necrotic tissue to make it impossible to convert urine with isoniazid alone, just as it was impossible with streptomycin. Patient's BUN dropped from 100 mg. down to 25 mg. during isoniazid therapy, however, demonstrating that drug is not toxic for nephrons. This is patient's only kidney and he is living on few pyramids at bottom end of kidney.

DRUG RESISTANCE

Every effort was made to prevent the development of resistance to streptomycin or PAS. Streptomycin was never given alone, but was always given with an adjuvant drug such as PAS, terramycin, promizole or tibione. This helped to delay the development of resistance.

Nevertheless, streptomycin did appear to exert some beneficial effect even after the patient's organisms were reported by the laboratory to be completely refractory to streptomycin. It is to be hoped that new drugs such as Isoniazid can be added to the combination of streptomycin and PAS, to reduce the incidence of drug resistance to all three of these medications.

SURGERY WITH CHEMOTHERAPY

Since large fibrous and necrotic lesions appeared to respond to neither streptomycin, PAS or isoniazid, it was still felt by this group that the best treatment for unilateral fibrocasesous renal tuberculosis was nephrectomy. In certain cases, where the disease was limited to one portion of the kidney, that portion was successfully excised by partial nephrectomy (fig. 4) under the "cover" of chemotherapy. Since all such operations carry with them a certain danger of dissemination of the organisms through the blood stream, these operations were "covered" with a higher dosage of streptomycin, namely 0.5 gm. every 6 hours for a period of 1 week, and PAS given by clysis or infusion at the rate of 20 gm. every 12 hours for 2 or 3 days immediately after operation. After that time the dosage was reduced to the standard regimen of streptomycin every third day and PAS daily, by mouth, and was kept up until pyuria disappeared.

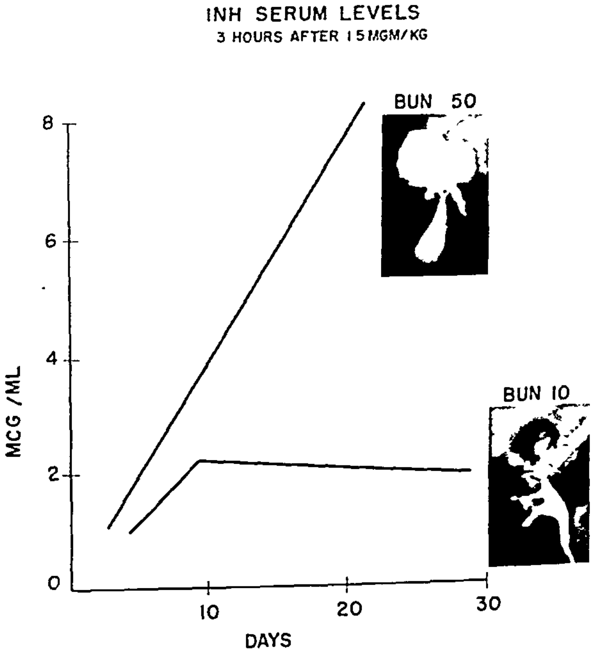

Fig. 6. Blood levels of isoniazid rose to toxic levels when drug was given to patients whose kidney damage was so extensive (top) as to cause elevation of BUN to 50 mg. Patients whose kidney damage was less extensive (bottom) and whose BUN was normal, showed no elevation of blood levels and no toxicity.

ISONIAZID (ISO-NICOTINIC ACID HYDRAZID)

In February 1952, we were informed by the newspapers of a new "wonder drug" for tuberculosis. The name of this drug is isoniazid (iso-nicotinic acid hydrazide). It is 600 times more powerful than PAS and appears more powerful than streptomycin in killing tubercle bacilli, at least in the test tube. Whether or not it will be as effective in vivo remains to be seen. Isoniazid does have a place in the treatment of renal tuberculosis. Like streptomycin, it brings about a gradual improvement in the cystoscopic appearance of the lesions of tuberculous cystitis, and can make the urine culture sterile for tubercle bacilli in some patients. It is an excellent drug for the treatment of streptomycin-resistant cases. It is not toxic for the nephrons. One of our patients, who is living on only three renal pyramids (fig. 5) has shown a fall of BUN from 100 mg. down to 25 mg. during isoniazid therapy.

However, when used alone, isoniazid appears to have the same limitations as streptomycin, plus a danger all its own. First, the presence of large amounts of necrotic tissue renders the drug ineffectual in sterilizing the urine from massive kidney lesions (fig. 5). Resistance to the drug may be developed by the tubercle bacilli in from two to eight weeks. In fact, spontaneous resistance (to 5 mcg/ml of isoniazid) was present in 4 out of our first 12 patients, even before the drug was given. The possible reversibility of this resistance is now being studied. Furthermore, a precaution must be taken with Isoniazid which was not necessary with streptomycin-PAS. In uremic patients this drug will accumulate in the blood when kidney excretion is impaired (fig. 6). At high blood concentrations Isoniazid may become a convulsant. Hyperreflexia, muscle twitching, spasm of the sphincters, and serious convulsions may occur. Liver damage may also be caused. Very high blood levels may accumulate, moreover, without any premonitory increase in symptoms. Hyperreflexia is not a true index to the blood level and cannot be depended upon as a warning sign of impending toxicity. This drug should not be given to epileptic patients. Sphincter spasm can be controlled by administering Banthine.

Isoniazid may be very effective, nevertheless, in the treatment of uremic patients with advanced kidney tuberculosis, but the precaution of doing blood levels on these patients is absolutely necessary.

DOSAGE AND DURATION OF TREATMENT

The optimum treatment regimen for isoniazid is as yet undetermined. The dosage can best be prescribed by determining the drug sensitivity of the patient's tubercle bacilli before treatment is begun. Doses of 3 mg. per kg. per day, divided into 2 doses, give blood levels of from 1 to 2 mg. per ml. This is adequate for most patients and is nontoxic. However, if pre-treatment resistance to 5 mg. or more is found, the dosage must be increased sharply to attain higher peak blood levels. The optimum duration of treatment with Isoniazid is completely undetermined. In view of the fact that resistance to the drug can develop within two to eight weeks if it is used alone, it may prove desirable to give this drug intermittently and probably in combination with PAS and streptomycin. All three drugs appear to have different modes of action. Since the streptomycin-PAS program appears to be effective for periods of at least 1 year, it would seem reasonable that a combination of all three drugs might be kept up in the same manner for the same length of time. In this way the effectiveness of the thoroughly proven streptomycin-PAS treatment may be enhanced, and the development of drug-resistance deferred. The possible hazards of this regimen are now being explored.

One tentative dosage plan is now being investigated is as follows: Streptomycin 1 gm. in 1 injection every third day, plus isoniazid 150 mg. every 12 hours. In certain severe cases the streptomycin is given at the rate of 1 gm. every 24 hours. Patients who can tolerate it can be given PAS 3 gm. 4 times daily, in addition to Isoniazid and streptomycin. However, patients who are at all unstable do not tolerate the loose bowel movements and intestinal gas which often accompany PAS.

SUMMARY

Streptomycin and PAS, in combination, have been used in 458 cases of genitourinary tuberculosis during the past 5 years and were effective in slowing the progress of the disease, even when the urine could not be sterilized. Survival rates among these patients were impressive.

Inoperable, bilateral renal tuberculosis was treated at this center, therefore, with from one to three years of intermittent combined therapy (PAS 12 gm. daily, plus streptomycin 1 gm. 2 times per week).

Unilateral, destructive renal tuberculosis, visible by x-ray, where the contralateral innocent kidney showed no pus cells and no tubercle bacilli in the ureteral urine, was treated by nephrectomy. In occasional cases partial nephrectomy proved practical, when combined with chemotherapy. Chemotherapeutic "coverage" was continued after all operations until pyuria ceased.

Isoniazid (iso-nicotinic acid hydrazide) is effective in improving the bladder lesions of renal tuberculosis. It does cause the urine culture to become negative in some patients. It is not nephrotoxic. Optimum dosage and duration of treatment are as yet undetermined.

Limitations of isoniazid appear to be the same as with streptomycin, if the drug is used alone. Drug resistance may develop after from 4 to 8 weeks, and the urine from large necrotic kidney lesions cannot always be sterilized.

An important precaution is necessary in patients with nitrogen retention. Isoniazid accumulates in the blood in these patients, and blood levels should be done in order to prevent serious convulsions. Hyperreflexia is not a true index to the blood level and cannot be depended upon as a warning sign of impending toxicity. Where blood levels can be done, this drug can be an important addition to the treatment even of uremic patients with massive kidney lesions.

Drug resistance was the most important limiting factor in the effectiveness of streptomycin, PAS and isoniazid. Since the mode of action of all three drugs appears to be different, it is reasonable to assume that a combination of these three potent drugs may greatly increase their effectiveness and further defer the development of drug resistance.

Five years of follow-up with bacteriological, symptomatic, x-ray and survival information appeared to justify the conclusion that modern chemotherapy can at least modify the lethal course of renal tuberculosis.

Our bacteriologists, Dr. Michael Kenney, and Milton Goldman, head nurse Lydia R. Sechler and her staff, our secretary Miss Alfreda Jastremski, illustrators Nakamura, Shapiro, and staff, and the Departments of Roentgenology and Urology have been most helpful in this work.

We wish to express our appreciation to Consultant Dr. Archie L. Dean for sponsoring this presentation.

The Harkness Pavilion, New York 32, N. Y.

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A NEW TYPE OF ARTIFICIAL KIDNEY. II. TREATMENT OF ACUTE AND CHRONIC UREMIA

GEORGE HOLLANDER, JULIAN A. STERLING AND JOSEPH C. DOANE

From the Departments of Medicine and Surgery, Albert Einstein Medical Center (Northern Division), Philadelphia, Pa.

Acute renal insufficiency can occur during degenerative renal disease or may be secondary to acute renal trauma, when there is prolonged hypertension and renal anoxia. It may also be produced by the ingestion of bichloride of mercury and similar poisons, by sulfonamide crystals and by scores of other mechanisms. Its presence may be easily recognized. The early stages of nephron deficiency should be suspected when the urinary output is less than twenty cubic centimeters per hour or when no urine has been passed for 12 hours. Additional indications of this state are the presence of an acid urine of low (less than 1.010) fixed specific gravity, albuminuria, increasing azotemia and often increasing hypertension. Other symptoms may exist which are usually cerebral and are due to decompensatory changes in the cardiovascular system. The signs of early renal failure may appear following excessive vomiting after surgery, prolonged shock-like states and blood transfusion reactions.

The treatment of acute renal insufficiency is based on the fact that kidney damage may be reversible because of the known regenerative ability of renal tissue. But by the same token, successful treatment must be based on a thorough and practical knowledge of renal physiology. Prevention of renal overwork by the reduction of protein metabolism is accomplished by feeding a high caloric, low protein diet. For an average person with renal insufficiency an intake of 10 to 20 gm. of protein a day is adequate if the total caloric intake is at least 1600 calories. This would prevent the use of intrinsic body protein.

The maintenance of fluid and electrolyte balance is important because the ability of the kidney to excrete water varies with the degree of renal damage. With oliguria or anuria, fluid administration is restricted; but at the same time adequate fluid should be given to keep the patient hydrated. The amount should be sufficient only to replace the fluid loss by respiration, vomiting, perspiration, and that lost through the urine and feces. If the original condition causing the anuria is accompanied by blood loss, dehydration or shock, administration of of fluids, blood or plasma may be indicated. An increased urinary output during recovery should be matched with an corresponding increase in the fluid intake.

Correct control of the body's electrolyte balance should be guided by the ability of the kidney to excrete sodium or chloride ions. Frequent measurements of the carbon dioxide combining power, sodium chloride and potassium levels in the blood are the guides which indicate the course of treatment. Careful replacement of lost ions is indicated. Acidosis may be controlled by a high caloric intake or by sodium bicarbonate given orally or intravenously. Potassium retention may be corrected by oral administration of the exchange resins. In this connection it

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should be remembered that stored blood may have a high plasma concentration of potassium due to passage of potassium from the red cells to the plasma. Clinical evidence of edema, hypertension, or signs of cardiac insufficiency also indicate a restriction in salt intake.

Infection may promote protein breakdown and increase the uremia. Since patients with acute renal insufficiency are susceptible to infections, anti-bacterial drugs such as penicillin and aureomycin are given for both prevention and treatment. Sulfonamides or other agents which may produce renal irritation should be avoided.

With severe prolonged renal insufficiency, measures to encourage extrarenal excretion may be used. These include the artificial kidney, gastric or intestinal lavage or peritoneal dialysis. The use of the artificial kidney presents little danger in experienced hands. It is an effective medium for removing specific diffusible substances from the blood. This is accomplished by osmosis through a cellophane membrane. The complications most frequently encountered with its use are hemorrhage, due to the use of heparin, hemolysis due to manipulation of the blood, changes in blood pressure,. clotting in the filtration system, and pyrogenic reactions. Using either the Kolff type kidney[1, 2] or the stationary type of artificial kidney described by us,[3] these complications have been adequately controlled so that the procedure is both safe and successful.

CLINICAL EXPERIENCE WITH THE ARTIFICIAL KIDNEY

Under conservative measures of therapy the mortality of patients who have renal insufficiency has been decreased greatly. In patients who have been treated conservatively without improvement, patients who have been overenthusiastically treated with water, electrolytes, renal sympathectomy and other methods to no avail, the use of the artificial kidney is indicated. Particularly so, since the risk to the patient is now negligible and since it does offer hope for a regained kidney function if such a possibility still exists. Any patient in severe acute or chronic uremia should be given the possible benefit of its use, since infection, nausea and vomiting, are likely to hasten an unfavorable outcome unless action replaces conservatism. It should not be used as a last resort in a moribund patient with little chance for recovery.

The use of the artificial kidney previously described[3] requires only the temporary loss from the patient of 150 to 200 cc of blood at any one time. Even this amount can be adjusted by varying the capacity of the kidney. While our apparatus gives a lower volume of blood flow than the Kolff type kidney it has the added advantage of increased safety by giving a better adaptation to the patient's cardiovascular system and blood volume. Thus it lessens the tendency to produce shock, especially in a patient with a small plasma volume. For its use with children, fewer plates can be used in the apparatus so that only a relatively small

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[1] Kolff, W. J.: Artificial kidney. Clev. Clin. Quart., **17:** 216, 1950.

[2] Merrill, J. P., Thorn, G. W., Walter, C. W., Callahan, E. J. and Hollingsworth Smith, Jr., L.: Use of an artificial kidney. I. technique. J. Clin. Invest., **29:** 412, 1950.

[3] Hollander, G., Sterling, J. A. and Doane, J. C.: New type of artificial kidney. I. Technique. J. Urol., **69:** 605, 1953.

TABLE I

EXP NO	PATIENT	SEX	AGE	DIAGNOSIS	INITIAL UREA VALUE IN MG %	FINAL UREA VALUE IN MG %	DURATION OF DIALYSIS IN HOURS	REMARKS
1	Dog			Uremia secondary to tying ureters, 3 days previously	269	225	1	No reactions
2	Dog			Uremia secondary to tying ureters	275	221	1½	No reactions
3	Dog			Uremia secondary to tying ureters	152	136	3	No reactions
1	R. B.	F	60	Rt. hydronephrosis; retroperitoneal reticulum cell sarcoma	92	16	2	Renal output increased from 320 cc to 1080 cc in 24 hours
2	T. S.	M	52	Chr. glomerulonephritis	160	102	1	No reactions
3	C. H.	F	67	Hepatorenal syndrome. Postoperative cholecystectomy. Oliguria	153	120	1½	Procedure stopped because of leak in cellophane
4	H. F.	M	46	Chr. cardiovascular renal disease. Pulmonary edema.	168	146	1	Coma and pulmonary edema relieved
5	E. R.	F	36	Convalescent typhoid fever. Transfusion reaction.	(N P.N. 150)	(N.P.N. 55)	8	Temporary improvement, regained consciousness. Died 5 days later.
6	E. W.	F	80	Arteriosclerotic cardiovascular renal disease. Postoperative appendicitis	116	—	1½	Developed shock and died during procedure.
7	A. M.	F	43	Hypertension; right hydronephrosis. Postoperative nephrectomy; oliguria	100	51	3½	Rise in blood pressure. Died during procedure from cerebral hemorrhage.
8	M. M.	M	45	Polysystic kidney disease	156	—	2	Rise in blood pressure. Chill during procedure. Died 4 days later.

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CLINICAL EXPERIENCE WITH THE ARTIFICIAL KIDNEY

Under conservative measures of therapy the mortality of patients who have renal insufficiency has been decreased greatly. In patients who have been treated conservatively without improvement, patients who have been overenthusiastically treated with water, electrolytes, renal sympathectomy and other methods to no avail, the use of the artificial kidney is indicated. Particularly so, since the risk to the patient is now negligible and since it does offer hope for a regained kidney function if such a possibility still exists. Any patient in severe acute or chronic uremia should be given the possible benefit of its use, since infection, nausea and vomiting, are likely to hasten an unfavorable outcome unless action replaces conservatism. It should not be used as a last resort in a moribund patient with little chance for recovery.

The use of the artificial kidney previously described[3] requires only the temporary loss from the patient of 150 to 200 cc of blood at any one time. Even this amount can be adjusted by varying the capacity of the kidney. While our apparatus gives a lower volume of blood flow than the Kolff type kidney it has the added advantage of increased safety by giving a better adaptation to the patient's cardiovascular system and blood volume. Thus it lessens the tendency to produce shock, especially in a patient with a small plasma volume. For its use with children, fewer plates can be used in the apparatus so that only a relatively small

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TABLE 1

EXP NO	PATIENT	SEX	AGE	DIAGNOSIS	INITIAL UREA VALUE IN MG %	FINAL UREA VALUE IN MG %	DURATION OF DIALYSIS IN HOURS	REMARKS
1	Dog			Uremia secondary to tying ureters, 3 days previously	269	225	1	No reactions
2	Dog			Uremia secondary to tying ureters	275	224	1½	No reactions
3	Dog			Uremia secondary to tying ureters	152	136	3	No reactions
1	R. B.	F	66	Rt. hydronephrosis; retroperitoneal reticulum cell sarcoma	92	16	2	Renal output increased from 320 cc to 1080 cc in 24 hours
2	T. S.	M	52	Chr glomerulonephritis	160	102	1	No reactions
3	C. H.	F	67	Hepatorenal syndrome. Postoperative cholecystectomy Oliguria	153	120	1½	Procedure stopped because of leak in cellophane
4	H. F.	M	46	Chr. cardiovascular renal disease. Pulmonary edema.	168	146	4	Coma and pulmonary edema relieved
5	E. R.	F	36	Convalescent typhoid fever. Transfusion reaction.	(N P.N. 150)	(N.P.N. 55)	8	Temporary improvement, regained consciousness. Died 5 days later.
6	E. W.	F	80	Arteriosclerotic cardiovascular renal disease. Postoperative appendicitis	116	—	1½	Developed shock and died during procedure.
7	A. M.	F	43	Hypertension; right hydronephrosis. Postoperative nephrectomy; oliguria	100	54	3½	Rise in blood pressure. Died during procedure from cerebral hemorrhage.
8	M. M.	M	45	Polysystic kidney disease	156	—	2	Rise in blood pressure. Chill during procedure. Died 4 days later.

amount of blood is without the body at any one time. In our original experiments we used a ten blood chamber apparatus, which contained about 75 cc of blood, giving an approximate blood flow of 50 cc per minute though the kidney. With this we were able to remove up to 3.8 gm. of urea per hour from the blood stream (table 1). We have attempted to increase this amount by doubling the capacity of the apparatus by doubling the number of chambers in the machine. The amount of retention products recovered depends upon the underlying pathological condition of the patient, the concentration of these metabolic substances in the blood, the duration of dialysis, the blood and perfusate flow through the apparatus and the temperature of the perfusate. There may be frequently a discrepancy observed between the observed and calculated drop in the blood urea nitrogen. This has also been observed by others.[4, 5] This apparently has some relationship to the duration of the uremia, occurring more frequently in chronic renal insufficiency than in the acute form. The amounts of urea obtained in our series (table 2) varied from 0.7 to 3.8 gm. cleared per hour.

TABLE 2

EXPERIMENT NUMBER	TOTAL UREA REMOVED DURING DIALYSIS IN GRAMS	UREA CLEARED PER HOUR IN GRAMS
Dog	2.4	2.4
Dog	2.7	1.8
Dog	2.8	.93
2	1.4	.7
3	2.56	1.7
4	7 2	1.8
5	30.0	3.8
6	3.6	2.4

CASE REPORTS

Acute renal insufficiency accompanying disease. Occasional renal failure occurs in many instances where irreversible changes cannot be demonstrated. These include previously healthy individuals whose anuria is a result of transfusions with incompatible blood, sulfonamide intoxication, renal injury from poisoning with heavy metals or other substances, and hemolytic reactions. Here the hazardous and rapid accumulation of nitrogenous and other waste products is readily amenable to artificial removal which may be life saving.

E. R., a 36 year old woman, was admitted to the hospital suffering from diarrhea and fever. Positive stool cultures of B. typhosis were obtained and treatment started with chloromycetin. The patient improved and over the next 2 weeks 3 blood transfusions were given. Excretory urography showed normal renal function and anatomy. On her twenty-first hospital day, the patient complained of left flank pain. Urine volume was more than 1000 cc daily. Urine culture showed Aerobacter aerogenes. Soon after the appearance of pain in the left

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flank, a bluish cyanosis was seen unaccompanied by obvious icterus. The impression was that the patient was having an episode of nonspecific methemoglobinemia. There was no chest pain or hemoptysis. A slight fever was present. The next day pain appeared in the right flank, accompanied by renal shutdown. A total of 50 cc of urine was passed on this day. The urine contained hemoglobin. Complete anuria now developed. Two days of treatment with ACTH produced no effect. The blood pressure which had been previously normal rose to 180/100 simultaneously with the onset of convulsions and semi-stupor. There was no edema.

Laboratory studies showed nonprotein nitrogen of 150 mg. per cent, urea nitrogen 106 mg. per cent, carbon dioxide combining power of 30 volumes per cent, creatinine 4.95 mg. per cent, calcium 9.2 mg. per cent, prothrombin time 26 seconds (50 per cent) and coagulation time of 5 minutes.

Dialysis with the artificial kidney was started and continued for 8 hours. It was discontinued because the patient's blood pressure was sustained at 90/70, which was felt did not provide efficient filtration pressure. The patient was clinically improved by the hematodialysis. Approximately 10 cc of urine was obtained during the procedure. The patient was restored to consciousness and there were no further convulsions. Her temperature, pulse and respiration were normal. Nonprotein nitrogen at the conclusion of dialysis was 55 mg. per cent.

The patient did well for the next 3 days although no urine was passed, when following a sudden episode of hypotension and fainting, she became comatose for 4 hours and died. Autopsy showed death to be due to a bilateral renal vein thrombosis.

Renal insufficiency accompanying injury. Patients in this group may fall into a different category than those previously healthy individuals who develop acute renal shut-down. Here the anuria may be precipitated by severe trauma and can follow surgical procedures. These patients are usually elderly and debilitated, whose postoperative course may be further complicated by vomiting, shock and coma. It is in these individuals that the artificial kidney is indicated, even if the situation might eventually respond to conservative therapy, in order to facilitate medical management and to decrease the strain on the patient.

C. H., a 67 year old white woman with a previous history of jaundice and typical gallbladder attacks, entered the hospital. A cholecystogram showed the presence of calculi and a cholecystectomy was performed. Three days postoperative her urinary output dropped to 10 cc, compared to an intake of 3800 cc. The blood urea nitrogen at this time was 52.7 mg. per cent. Her oliguria persisted for the next 2 days despite intakes ranging from 3000 to 3750 cc per day. At the time dialysis was started her temperature was 102.2F, blood urea nitrogen was 153 mg. per cent. The patient was comatose and clinically pulmonary edema was present. Dialysis was continued for 1½ hours and was stopped because of a leak in the cellophane. At the end of the procedure the blood urea nitrogen was 120 mg. per cent and 2.56 gm. of urea was recovered in the perfusing fluid. During the procedure the patient voided 40 cc of urine compared to 10 cc for the previous 24 hours. The pulmonary edema improved. Notwithstanding, the course was progressively downhill and 2 days later the urea nitrogen was 159 mg. per cent. The patient died 3 days after dialysis.

Uremia with acute or chronic renal disease. Many of the untoward symptoms of chronic uremia may be relieved by dialysis. Acute exacerbations of glomerulonephritis, infections, nausea and vomiting and acidosis may be the forerunner of terminal uremia. Even though after dialysis there may be a rapid re-accumulation of the nitrogenous waste products, the increase in well being may facilitate proper dietary management and the correction of acidosis, making the patient more comfortable. Preoperative use of the artificial kidney is also indicated in toxic uremic patients who are to undergo surgical procedure.

R. B., a 66 year old white woman, was admitted with the diagnosis of retroperitoneal reticulum cell sarcoma with osseous metastases. Genito-urinary evaluation indicated a right hydronephrosis with kinking at the ureteropelvic junction. Her blood pressure was 174/84. During her hospital stay the patient became progressively lethargic and unresponsive, with a marked decrease in her urinary output. The blood urea nitrogen was 92 mg. per cent. Dialysis with the artificial kidney was continued for 2 hours. Hypotension developed and the procedure was discontinued. The patient's final reading at this time was a blood urea nitrogen of 16 milligrams per cent. The renal output increased from 320 cc to 1080 cc for the next 24 hours and was maintained thereafter at more than 1000 cc daily. Following this extrarenal hematodialysis the patient's urea nitrogen remained between 42 and 50 mg. per cent until her death 1 month later because of a subarachnoid hemorrhage.

Uremia with congestive heart failure and pulmonary edema. Congestive heart failure with pulmonary edema in uremia can be relieved with extrarenal dialysis. This complication may result from either administration of excessive fluid or directly due to the toxic effects of the uremia upon the cardiovascular system. While the mechanism of relief is not clear it is possibly due to a combination of dehydration and correction of the electrolytic balance.

H. F., a man aged 45 years, had arteriosclerotic cardiovascular renal disease for 15 years. During the past 3 years renal function had decreased and the urea nitrogen continued to climb along with an elevation in the blood pressure. For the 9 months previous to the present admission he had severe anemia accompanied by decreasing urinary output. On the day the artificial kidney was operated the patient was semi-comatose. He had been previously digitalized, but despite this, clinical evidence of pulmonary edema was present. The blood urea nitrogen was 168 mg. per cent, carbon dioxide combining power was 15 volumes per cent and the 24 hour urine output measured 300 cc. The apparatus worked for 4 hours with two slight drops in blood pressure. Clinically the pulmonary edema improved and the patient became more alert. At the conclusion of the procedure the blood urea nitrogen was 146 mg. per cent and the carbon dioxide combining power rose to 31 volumes per cent. His urinary output increased to over 500 cc per day. Examination of the dialysate indicated that 7.2 gm. of urea nitrogen had been removed from the plasma of the patient. Despite this temporary improvement, the uremia persisted and the patient died one week later.

SUMMARY

The management of patients who suffer acute renal insufficiency is planned to correct physiological alterations taking place during the illness. An analysis of each case is needed. Diet, fluid and electrolyte administration and infection must be controlled as indicated by the condition of the patient and a knowledge of the chemical changes taking place.

General management of renal insufficiency as well as the specific use of artificial hematodialysis by means of an artificial kidney has been discussed.

The use of the artificial kidney in eight cases has been presented. Differences in management have been discussed for patients with acute renal insufficiency secondary to (a) infectious or degenerative disease other than the kidney, (b) trauma, (c) acute and chronic renal disease and (d) cardiac failure accompanying renal disease.

The artificial kidney is not permanently useful in chronic renal disease with loss of renal reserve and regenerative ability. It finds its greatest use in renal shutdown following such conditions as hemorrhage, transfusion reactions and mercury poisoning.

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SPONTANEOUS NEPHRODUODENAL FISTULA: REVIEW OF THE LITERATURE AND REPORT OF A CASE

GEORGE H. JONES, OAKLEY A. MELENDY AND WILLIAM F. FLYNN

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The spontaneous occurrence of a nephroduodenal fistula is a rare clinical entity. Examination of the records of the Boston City Hospital reveals no instance of this diagnosis in the clinical archives. Thorough search of the literature yields seven such cases. The rarity of this condition and the previously unrecorded primary changes encountered by the authors prompts this brief summary of the literature and case report.

King in 1950 reported a case successfully treated by nephrectomy and closure of the fistulous tract. The following table (after King) summarizes the known cases and includes the present case:

CASE	YEAR	SEX	AGE	ETIOLOGY	TREATMENT	OUTCOME
1. Rayer	1839	F	45	?	Conservative	Died
2. Barlow	1843	F	26	Hydatid cysts	Conservative	Died
3. Bang	1874	F	22	Tuberculosis	Conservative	Died
4. Turner	1893	M	18	Tuberculosis	Conservative	Died
5. Pulvertaft	1935	F	28	Tuberculosis with calculi	Conservative	Died
6. Biondi	1935	F	28	Tuberculosis; ? perforated ulcer	Operative	Satisfactory
7. King	1950	M	62	Pyelonephritis and perinephritis	Operative	Satisfactory
8. Present case		F	65	Epidermoid CA and calculus	Operative	Died

The literature further reveals a case incompletely reported by Fernelius in 1646 and an interesting ureteroduodenal fistula originating from the ureteropelvic junction recorded by Davis.

The predominant cause of this type of fistula formation has been tuberculosis; however, any disease process escaping the confines of the perirenal fascia can conceivably rupture into the intestinal tract.

Gastro-intestinal complaints predominate the symptomatology of this condition. Severe nausea, vomiting, epigastric pain, diarrhea, flank pain and weight loss are common. Dysuria, frequency, burning and pyuria may also occur either prior to, in conjunction with, or after the onset of the intestinal symptoms.

Physical examination uniformly discloses a patient in poor nutritional balance with or without a palpable mass in the right upper quadrant or flank. In one of the reported cases pressure on a right flank mass initiated vomiting of uriniferous material and a decrease in the size of the mass.

The clinical diagnosis of nephroduodenal fistula rests in the roentgen demon-

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stration of the fistulous tract connecting the kidney and the duodenum. This may be accomplished by excretory urography if the kidney functions, retrograde pyelography or the extraduodenal extrusion of barium during the examination of the upper gastro-intestinal tract.

CASE REPORT

E. P., a 65 year old white woman, was admitted to the Boston City Hospital March 9, 1951 complaining of weakness and anorexia gradually increasing in severity for the preceding 10 months. A 10 pound weight loss had been noted recently. Intermittent dull aching pain in the right flank began 4 months prior to admission and frequency, urgency and pyuria developed 4 weeks before she sought medical attention.

FIG. 1. Right pyelogram showing flow of dye into duodenum.

The salient features of the physical examination were: malnourishment, mild hepatomegaly and a 10 cm. mass in the right upper quadrant extending toward the right flank. The temperature on admission was 99.6F and low grade pyrexia continued.

The laboratory studies were as follows: Hematocrit 38.5; leukocytes 22,600 with a slight shift to the left; blood urea nitrogen 25; carbon dioxide combining power 65 per cent; chlorides 92; cephalin flocculation 1 plus and 28 per cent bromsulfalein retention in forty-five minutes. Repeated stool examinations showed traces of blood on three occasions.

Roentgenologic studies were reported as follows: Graham series showed faint filling of a moderately enlarged gallbladder with fair contraction after a fatty meal. A large laminated calcific shadow was noted outside the confines of the gallbladder outline. Examination of the stomach and upper intestinal tract

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proven. Despite all supportive measures the patient followed a steady downhill course and expired on the fifteenth postoperative day.

The salient features of the autopsy examination were as follows (Dr. R. Gilchrist): Exploration of the operative site revealed the enterostomy intact and the previous opening into the duodenum completely sealed, although the fistulous tract toward the renal area was easily demonstrable. The kidney was involved in a dense mass of tissue and in the process of its removal the calculus was discovered in what remained of the renal pelvis. There was no definite communication of the tumor with the pancreas as had been suspected at the time of operation. The renal parenchyma was largely replaced by brown-gray tumor tissue, a plug of which protruded into the vena cava.

Microscopy showed epidermoid carcinoma of the kidney with evidence of neoplastic invasion along the suture line of the ulcerated area in the duodenum. There was no evidence of metastatic spread in other tissues examined. The final report on the tissue was epidermoid carcinoma originating in the kidney and involving the duodenum (fig. 2).

DISCUSSION

Satisfactory results in the treatment of nephroduodenal fistula have been obtained in only two recorded instances and these were accomplished by surgical intervention. (Biondi; King.) Although the case herein reported ended in death it is the opinion of the authors that closure or excision of the fistulous tract and removal of the diseased kidney are necessary if the patient is to receive the maximum benefit of treatment.

SUMMARY

The literature dealing with spontaneous nephroduodenal fistula is briefly reviewed and an additional case secondary to epidermoid carcinoma and renal calculus is reported.

Although the recorded evidence is scant, the treatment of choice would appear to be excision or closure of the fistulous tract and nephrectomy. Reports of the successful treatment of similar cases should clarify the solution of this unusual clinical problem.

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showed a small ulcer crater on the lower third of the lesser curvature of the stomach, narrowing of the antral portion of the duodenal loop and extrinsic pressure on the right posterior portion of the second portion of the duodenum suggestive of a retroperitoneal mass. Excretory urography disclosed a normal appearing left kidney and an indefinite mass in the region of the right kidney without dye appearance in this area at the end of 45 minutes. The previously mentioned calcific shadow seemed to be in the position of the right kidney mass on the oblique and anteroposterior views. Ureteral catheterization on the right side revealed obstruction at 21 cm. from the ureterovesical juncture. Retrograde pyelography showed a trickle of contrast medium extending toward the calcific density and prompt appearance of the dye in the duodenum (fig. 1).

In view of the nephroduodenal fistula demonstrated by the retrograde studies the following diagnoses were entertained: perinephritic abscess secondary to calculus pyonephrosis, epidermoid carcinoma of the kidney secondary to calculus, or tuberculosis with calculus, although the type of calcification was not that commonly seen with tuberculosis.

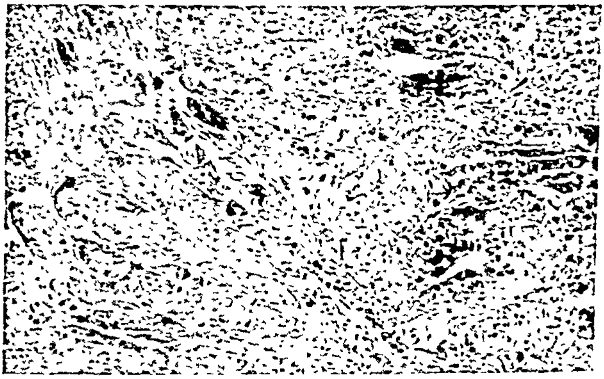

FIG. 2. Photomicrograph × 80. Portion of fistulous tract showing cords of epidermoid cells in fibrous tissue stroma. Similar cells found in renal substance and along suture line of duodenal repair.

Closure of the fistulous tract seemed mandatory as the initial procedure in this case and accordingly the patient was prepared and explored through a right rectus incision. The liver was normal. The mass previously palpated was found to be adherent gastrohepatic ligament, transverse colon, duodenum and right kidney. The structures were separated and the duodenum opened, revealing an ulcerated area on the posterior surface extending toward the kidney and cephalad toward the pancreas. It was believed that removal of the kidney was technically impossible due to the fixation of the tissues. A biopsy of the tract extending from the duodenum was reported as epidermoid carcinoma by frozen section. The opening in the duodenum was then closed in two layers and a retrocolic posterior gastro-enterostomy to prevent further duodenal obstruction was done. The patient drained copious amounts of seropurulent material postoperatively. This was thought to be duodenal contents but could not be definitely cell nidus in the genital ridge. As we mentioned previously, with so much development and metamorphosis happening in such a brief period during embryonic development, we wonder that aberrations do not occur more frequently.

CASE HISTORY AND CORRELATION OF FINDINGS

A white woman, aged 71, entered the Illinois Masonic Hospital (Case No. 127106) January 17, 1951. Her chief complaints were moderate pain in the right flank and costovertebral angle, protracted weakness, loss of energy and anorexia for the past 6 or 8 months. Her progressive loss of weight was rather alarming and the general overall picture was one of rapid retrogression. The right flank and costovertebral discomfort had been increasing in severity and sedation for its control had been used over a long period. Her temperature range had been rather constant, 100 to 102F, and oftentimes associated with chills. Constant headache, malaise and weakness were present. All household duties had accordingly been discontinued. The patient had no history of dysuria, frequency or hematuria.

The patient claimed to have had an operation on the right kidney a number of years previously and while the diagnosis was rather obscure, from her description in all probability it was a perirenal abscess. The incision appeared to be a large right rectus which obviously was a transperitoneal approach for some renal or perirenal suppuration. The reason for the transperitoneal approach was in her memory very vague. She had pneumonia 12 years ago. She had moderate constipation for 25 years. Menopause occurred at the age of 50.

The patient was a well developed, well nourished woman who showed no evidence of acute distress but was lethargic. The lung findings were within normal limits. The heart showed a slight left ventricular enlargement. The pulse was 76 and blood pressure 160/90. The abdomen was large and soft. Bowel sounds were normal. There was mild tenderness below the right costal margin laterally. There was a healed right rectus scar. On deep palpation the abdomen was not sensitive except in the area of the right flank and costovertebral area. There were extensive varicosities on both legs.

Laboratory findings: Urine: Specific gravity 1.018, reaction acid, no red blood cells; occasional white blood cells. The urine was singularly free of pathological elements.

Blood: Red cells 4,310,000; leukocytes 27,000; hemoglobin 10.5 gm. Differential count showed 90 per cent segmented form, 4 per cent lymphocytes, 6 per cent monocytes, 3 per cent eosinophils.

Blood chemistry: Nonprotein nitrogen 33 mg. per cent; urea nitrogen 70 mg. per cent; creatinine 1.5 mg. per cent, sugar 108 mg. per cent, total proteins 7.92 mg. per cent. Sedimentation rate 65 mm.

Cystoscopic analysis: The bladder, except for isolated areas of incrustation cystitis, appeared normal. There were no bladder deformities, tumors, stones or diverticula. The ureteral orifices were normal in appearance; however, no urinary efflux from right ureteral orifice was noted. The left ureteral catheter passed to left renal pelvis without obstruction. Urine studies were taken and pyelograms made. The right ureteral catheter was definitely obstructed at approximately the

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LEIOMYOSARCOMA IN RETROPERITONEAL FAT: AN EXTRAORDINARY ENTITY

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In general agreement with most authors as to the practical value and importance of reporting rare, exceptional and uncommon findings, we herewith present an interesting case of an infrequent, complicated tumor in an unusual area.

The retroperitoneal space is host to the most fantastic group of pathological entities, all of which are a definite challenge to one's imagination and diagnostic acumen. This may be because of its importance by location in the embryologic development of the renal, genital, neurological, vascular, muscular and lymphatic systems. Whatever the reason, here we find a diversity of neoplastic lesions which challenges the imagination of the oncologist, clinician, surgeon, anatomist and pathologist. A great number of neoplasms, cystic and solid, benign and malignant, have been found in the retroperitoneal space. The rarest of all has been the leiomyosarcoma. When one searches the medical literature and finds only three or four authentic cases, he realizes how uncommonly it occurs. We believe that some of the cases may have been reported under other classifications, either through improper identification or differences in diagnostic standards set by pathologists. However, that may be, we have found only 3 cases[1, 2, 3] and reference to a fourth, of retroperitoneal leiomyosarcoma in the world medical literature of the last half a century.[4, 5, 6, 7, 8, 9,]

According to definition, a leiomyosarcoma is a malignant tumor comprised entirely or almost entirely of tumor cells which have been derived from leiomyoblasts. Hence, theoretically, we should expect to find such a tumor in connection with any organ or tissue which contains smooth muscle cell. Such indeed we do find in the genital system, gastro-intestinal tract and the urinary system. Only 2 cases have been reported for the vascular system and both of these were in the inferior vena cava. When an isolated leiomyosarcoma is found in the retroperitoneal space, one first attempts to assign its origin to some organ in that region but is immediately stymied. It is not entirely improbable that such an entity may represent a teratoma or teratoid mass, arising in an aberrant embry-

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confirmed by a nephrostomy and indwelling de Pezzer catheter for drainage Penrose drains were liberally placed at the site of the empyemic ureter and the parts closed in layers around the nephrotomy tube

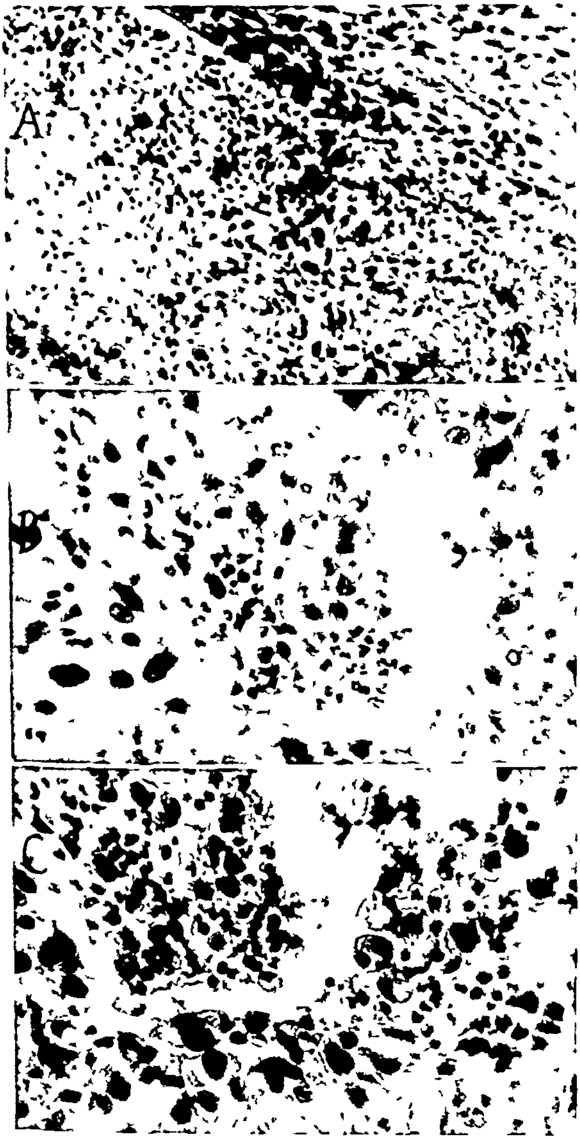

Fig 2

On February 12, 1951 the kidney and ureter were removed by a second stage ureteronephrectomy.

The patient was given the usual modern supportive measures, fluids and antipelvic brim and no urine was obtained; hence a functionless right kidney was assumed and later established.

Retrograde pyelograms of the urinary tract presented only slightly better filling of the renal pelvic structures on the left than was obtained by excretion studies. The silhouette of the left renal area was unaltered. No gross deformity was noted other than possibly slight contraction of the entire renal pelvic structures. Visualization of right kidney indicated a large impacted calculus lodged in the right ureter near the crest of the ilium, completely obstructing the ureter to contrast medium. Evidence of a probable large kidney shadow in low position was present, with a secondary calcification noted in the peripheral portion, probably an intrarenal calcification or calculus in this greatly enlarged kidney. See figure 1.

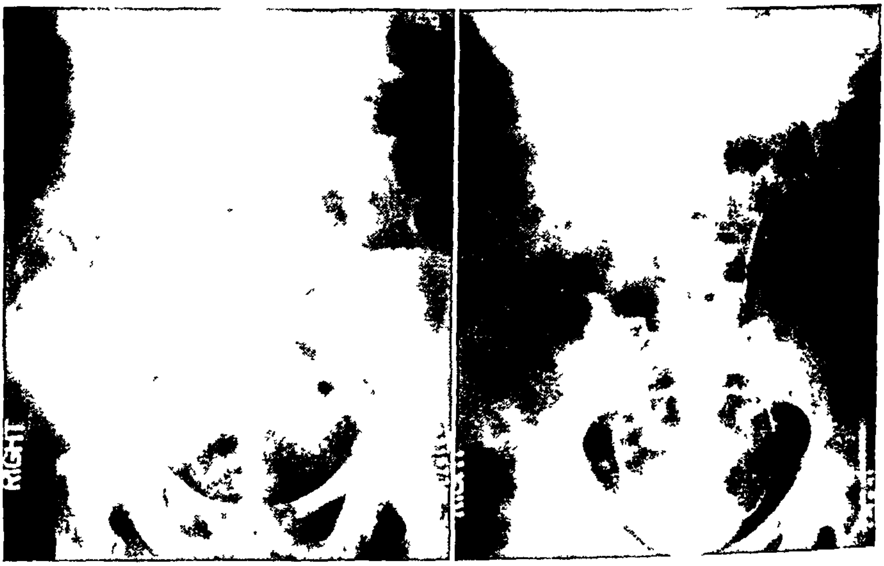

FIG. 1

Operation (*ureterotomy, nephrostomy, nephrectomy*): Under combined intravenous sodium pentothal and cyclopropane gaseous anesthesia, the kidney and ureter were exposed by the usual right posterior lumbar incision. The incision extended from the costovertebral angle across the right flank of the abdomen hence exposing the entire upper right urinary tract and ureter to the pelvic brim. A large impacted ureteral calculus at the pelvic brim had completely destroyed the ureter, giving a typical picture of ureteral necrosis and empyema. In exposing the kidney we removed large amounts of retroperitoneal fat. Two globular, soft and capsulated masses were incidentally exposed which were thought at first to be simple lipomas. The tumor masses were freely movable and apparently had not invaded surrounding structures. The kidney itself was tremendous in size, atrophic and advanced fibrous adhesions had adhered to surrounding structures. It appeared as a large hydropyelonephrosis which was confirmed by a nephrostomy and indwelling de Pezzer catheter for drainage Penrose drains were liberally placed at the site of the empyemic ureter and the parts closed in layers around the nephrotomy tube.

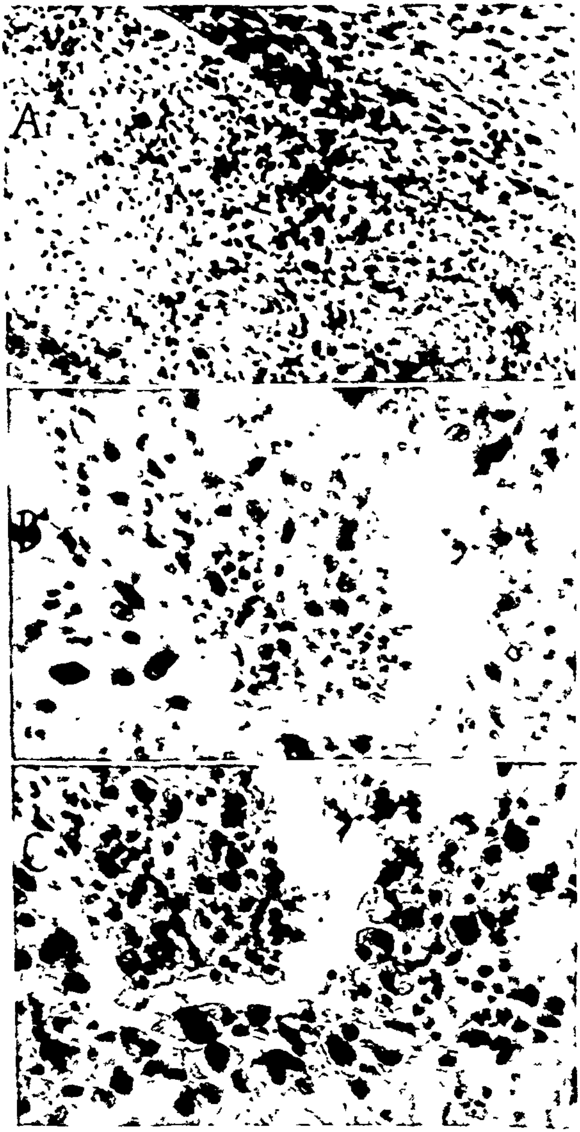

Fig. 2

On February 12, 1951 the kidney and ureter were removed by a second stage ureteronephrectomy.

The patient was given the usual modern supportive measures, fluids and antibiotics. After approximately ten days of temporary improvement of the febrile state, the toxicity and mounting blood value became overwhelming and the patient expired of bilateral hypostatic pulmonary congestion and uremia.

Pathology: The gross specimen consisted of two parts, first of which was 7.5 by 7 by 2.3 cm., within which were palpable two fleshy nodules. On section these nodules measured 3.2 by 3 by 2.7 cm., and 1.2 by 1.3 by 1 cm., respectively. These were of fleshy consistency with slightly bulging out surfaces of light tan color. The margins were well circumscribed. The remainder of the mass was comprised of normal appearing yellow adipose tissue.

The second part was a portion of adipose tissue 4 by 2.7 by 2.3 cm., with rough irregular surfaces. On one surface there was a partially opened, small sac-like structure 22 by 30 mm. in diameter, which contained a hard, gritty stone 22 by 7 by 5 mm. The wall of the sac was 1 mm. in thickness and the lining was roughened by numerous flat, thin, calcific plaques which gave the wall a variegated purple-yellow and tan character. Diagnosis: Large hydropyonephrotic atrophy. Sectional pieces examined microscopically revealed a mesenchymal sarcoma of the kidney.

Note: This extraordinary tumor showed abundant areas of primitive mesenchymal character, together with more differentiated tumor resembling, in part, muscle tissue, in part connected tissue. Some areas suggested liposarcoma and there were some zones which contained epithelial differentiations.

Microscopic diagnosis: Leiomyosarcoma in retroperitoneal fat; dense fibrous tissue with calcification and chronic inflammatory reaction.

Note: No renal tissue was recognizable. The origin of the renal sarcoma was not apparent. See figure 2.

SUMMARY

The purpose of this presentation is to report a case of leiomyosarcoma in retroperitoneal fat and to add another singular pathological entity to urological literature. The case presented a definite challenge which we feel merits conjecture.

The authors want to express their grateful appreciation to Dr. Lester King, Chief Pathologist, and Dr. John Gilmore, Chief of the Department of Roentgenology of the Illinois Masonic Hospital, for their helpful assistance in the preparation of this report.

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BILATERAL URETERAL OBSTRUCTION DUE TO ENVELOPMENT AND COMPRESSION BY AN INFLAMMATORY RETROPERITONEAL PROCESS

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In 1948, Ormond[1] reported 2 cases of ureteral obstruction due to a retroperitoneal inflammatory process. At that time he was unable to find a previously reported case. Ormond's first patient eventually died as a result of renal failure, but in the second case the involved portions of the ureters were freed from the mass and allowed to lie loosely in the peritoneal cavity, relieving the obstruction.

In 1949, Ewell and Bruskewitz[2] reported a third case, in which the left kidney was removed and the right ureter freed from the mass, with a good result.

I wish to present a fourth case, this patient also having been relieved by moving the midportion of each ureter to a position free in the peritoneal cavity.

F. S., a white man aged 51, first entered the Gulf, Colorado, and Santa Fe Hospital on May 14, 1950, with a complaint of pain in the small of the back and in both lower quadrants of the abdomen. He had been in good health until 2 months prior to his admission, when he had an acute illness of 1 weeks' duration, characterized by diarrhea, mild fever, and general malaise. It was during convalescence from this illness that he first noted a dull, aching pain in the lumbosacral region, radiating into the testicles. The testicular pain subsided, but the back pain continued to be present and was later associated with soreness and aching across the lower abdomen. For 2 weeks he had noted moderate abdominal distention, nocturia of 2 or 3 times, and slight burning on urination.

On physical examination he did not appear acutely ill. He was well developed, and his blood pressure was 135/105. Moderate tenderness was present throughout the lower abdomen. No masses were palpable. There was no tenderness in either costovertebral angle. The prostate was slightly enlarged, smooth, and boggy. The secretion showed pus cells, grade 2.

Because he continued to have a moderately severe, low-back pain, general malaise and weakness, the patient remained in the hospital for a period of 1 month. Many laboratory procedures were performed. The sedimentation rate was 23 mm. per hour (Westergren). A roentgenogram of the spine revealed narrowing of the lumbosacral joint space. A plain urogram and an excretory urogram made May 30, 1950 revealed normal kidneys with good drainage. Other laboratory studies done were all within normal range; these tests were: complete blood counts, urinalyses, Mazzini serological test, glucose tolerance test, serum lipase, gastric analysis, electrocardiogram, and roentgenographic studies of the stomach, gallbladder, colon, chest, and small bowel. The orthopedist, who saw him in consultation, did not believe that the back pain was due to skeletal changes.

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[1] Ormond, J. K.: J. Urol., 59: 1072–1079, 1948.

[2] Ewell, G. H. and Bruskewitz, H. W.: Urol. & Cutan. Rev., 56: 3–10, 1952.

The patient returned to the hospital 2 weeks later, on June 29, 1950, when, in addition to his other complaints, he had a constant, severe, aching pain in the left costovertebral angle, of 24 hours' duration. This pain radiated to the left lower quadrant and left testicle. He was acutely ill and required opiates for relief of pain. The temperature was 98.6F; the pulse rate was 96 per minute, and respiration was 20 per minute. The blood pressure was 156/94. The abdomen was distended and tympanitic, and there was slight tenderness throughout the abdomen. There was muscular rigidity and marked tenderness in the left costovertebral angle.

The hemoglobin was 13 gm. per 100 cc; the red cells numbered 4.4 million per cubic millimeter, the white cells 7,000, with 84 per cent polymorphonuclears, 12 per cent lymphocytes, and 4 per cent monocytes. The sedimentation rate was 88 mm. per hour (Westergren). The urine was clear, yellow, acid, with a specific gravity of 1.020, and contained an occasional pus cell. A plain urogram was negative. An excretory urogram revealed a normal right kidney, but no evidence of function on the left.

Cystoscopy was done the next day, and a 7F catheter passed easily to the left renal pelvis, with a resulting rapid flow of urine. The catheter was left indwelling for 72 hours. After removal of the catheter the patient had more severe, colicky pain and, in addition chills and fever. Although no difficulty was encountered in passing a catheter, my impression at that time was that the patient had a nonopaque ureteral calculus.

From July 5 to July 27, 1950, the patient was acutely ill. To control his pain, chills, and fever, he was given antibiotics of one type or another almost continually, and for a large part of the time he was on ureteral catheter drainage.

Pyelograms were made on July 5, 12, 18, and 25, 1950, each one being on the occasion of removal of an inlying catheter. These films consistently showed a mild pyelocaliectasis with slight dilation of the upper 4 or 5 cm. of the ureter, a very marked narrowing of the entire midportion of the ureter, and a normal outline of the lower 10 to 12 cm. of the ureter (fig. 1, *A*).

Although the patient's infection could be controlled by means of ureteral catheter drainage and antibiotics, it became obvious that the underlying cause of his ureteral obstruction was not resolving and was probably not due to an intrinsic lesion. The possibility of a retroperitoneal, inflammatory process, as described by Ormond, was considered; but, as the process was unilateral at the time, we also considered a retroperitoneal tumor of the lymphoblastoma group. Immediate drainage of the kidney was necessary, because of the marked infection present. For this reason a left loin exploration was done on July 27, 1950, and the ureter explored. The upper 5 cm. of the ureter was found to be slightly dilated; below that level, and as far as exploration could be carried, the ureter was completely surrounded by a mass of rubbery, indurated tissue. Several sections were removed for biopsy. The peritoneum was then opened, and on palpation a flat, but somewhat irregular mass, estimated to be 7 or 8 cm. in diameter and possibly 1.5 cm. in thickness, was found overlying the promontory of the sacrum. The peritoneum was closed, and a nephrostomy was done.

The tissue removed for biopsy was examined by Dr. Charles Phillips, who reported: "Study of this tissue, when fixed, shows that the process is one of some type of chronic inflammation with a considerable hyperplasia of connective tissue, during the process, of which a good many large and rather bizarre fibroblasts have been developed. These generally take an ovoid shape, but stain rather evenly and lightly as a rule. Collagen fibers formed during such growth have woven the matrix for the process, with the most characteristic feature being that of great numbers of lymphocytes scattered around and frequently gathered into small groups. The fatty part of this specimen is extensively infiltrated, as well as the firmer parts. Due consideration has been given to the possibility that this process may not be a simple inflammation, but that it may be a low-grade sarcoma of the fibroblastic type. Careful study, however, of all parts of the specimen shows only chronic inflammation." (See figure 2.)

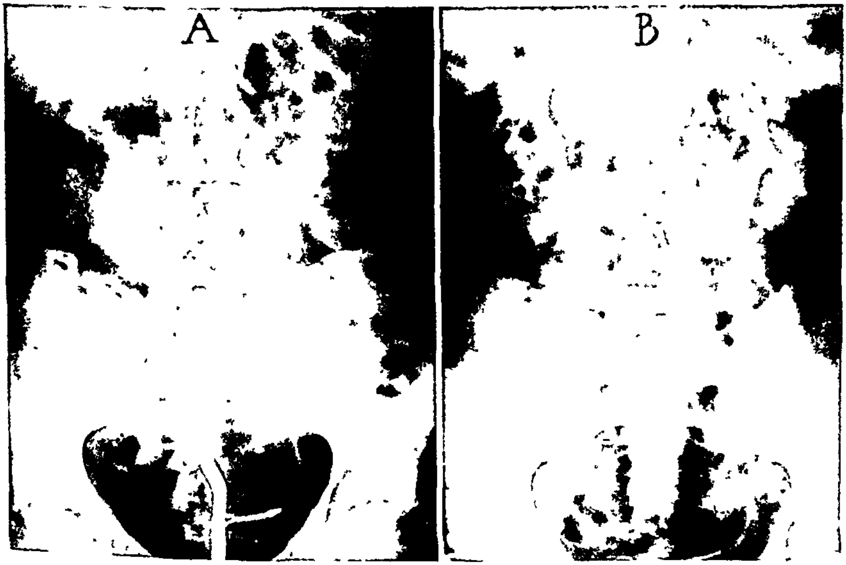

FIG 1

His convalescence following nephrostomy was satisfactory, although he was slow in regaining his strength. He was given roentgen therapy over the region of the granuloma for a dosage of 840 r. He was dismissed to his home on the twenty-first postoperative day, with the nephrostomy tube in place, and with advice to return later for abdominal exploration and attempt at freeing of the ureter.

He was seen every 2 weeks until October 3, 1950, when he re-entered the hospital for abdominal exploration. At that time the hemoglobin was 11.5 gm. per 100 cc; the red cells numbered 4 million per cubic millimeter, the white cells 6,550. The blood urea was 54 mg. per 100 cc. The urine contained pus cells, grade 1. An excretory urogram revealed, for the first time, dilation of the pelvis, calyces, and upper ureter on the right. The left side remained unchanged.

On October 9, 1950, a lower midline incision was made, going to the left of the umbilicus. A smooth, firm, rubbery mass was present, situated chiefly over the fifth lumbar vertebral body, obscuring the bifurcation of the aorta, and extending somewhat higher to the left of the vertebral column. This mass was about 8 or 9 cm. in diameter, with poorly defined edges, and was about 1.0 to 1.5 cm. in thickness.

The right ureter was exposed in its normal position rather deep in the pelvis An incision was made in the lateral peritoneum. The ureter was followed upward, and opposite the fifth lumbar vertebra it was found to be bound down for 4 cm. in the edge of the previously noted inflammatory mass. It was freed easily from the mass by blunt dissection. The middle 10 cm. of the ureter were allowed to remain free in the peritoneal cavity, and the peritoneum was closed behind the ureter.

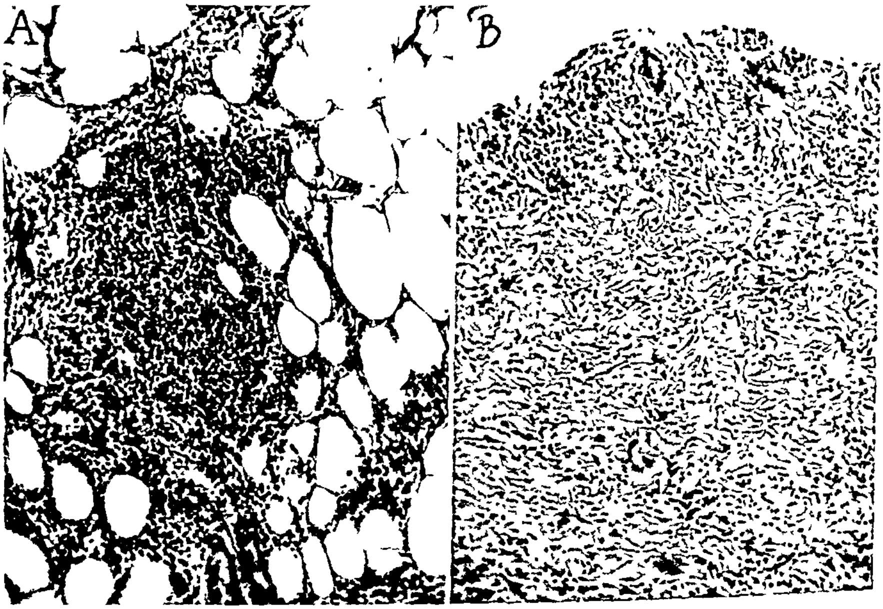

FIG. 2

The left ureter was exposed by an incision lateral to the sigmoid. It, too, was found to be bound down in the inflammatory tissue for 6 cm. It was freed from the mass and for 3 cm. above and below. Twelve cm. of the ureter were left free in the abdominal cavity, and the peritoneum was sutured posteriorly.

Specimens removed for biopsy from several areas in the retroperitoneal mass revealed microscopic findings identical with that removed at the time of nephrostomy.

During the first 5 postoperative days practically all urinary drainage was from the left nephrostomy tube. After that date there was a good output of urine from the bladder. The nephrostomy tube was removed on the fourteenth postoperative day. The sinus drained only 24 hours and then remained dry. The patient returned home on the seventeenth postoperative day, markedly improved. He returned to full duty as a general car foreman for the railroad on January 1, 1951, and has been completely relieved of all symptoms. He has returned for observation on November 14, 1950; December 4, 1950; March 26, 1951; and July 5, 1951.

Studies on the first 3 admissions were largely by means of excretory urogram, which revealed a gradually diminishing hydronephrosis on both sides. On July 5, 1951, more complete studies were made, including bilateral retrograde pyelograms, which revealed a rather tortuous course of both ureters, especially in that the midportion of each ureter was displaced laterally, but both were of normal caliber, and the pelves and calyces were of normal outline. (fig. 1, *B*) Delayed films revealed excellent drainage on both sides. The urine was clear; specific gravity was 1.022, with only a rare pus cell present. The hemoglobin was 15 gm. per 100 cc, and the red cells numbered 5 million. The blood urea was 48 mg. per 100 cc.

DISCUSSION

The etiology of this condition is obscure. The acute illness experienced by this patient 2 months prior to admission may well have represented the onset of the retroperitoneal, inflammatory lesion. Just what processes may have gone on during the 5 months from onset until the first biopsy specimen was obtained is conjectural. The fibrous nature of the material removed at operation may represent a stage in the healing of an acute, inflammatory process.

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ACCIDENTAL INJURY TO URETERS AND BLADDER IN PELVIC SURGERY

PAUL W. ASCHNER

Accidental injury to one or both ureters has probably occurred from the beginning of surgeon's efforts to eradicate disease of the female generative organs, and of the colon and rectum. The first nephrectomy by Simon in 1869 was for a uretero-abdominal fistula. Injury of the ureter during a Kraske operation was reported by vonRosthorn in 1895. In the same year Tuffier reported 40 instances of ureterovaginal fistula following vaginal hysterectomy. Data on the incidence of ureteral injury were reported by Sampson (1909) 30 in 4,672 pelvic operations; Wertheim (1913), 49 in 500 radical hysterectomies; Lenormant and Leibovici (1924), 8 in 800 hysterectomies; Stevens (1934), 4 in 1086 pelvic procedures; Newell (1939), 15 in 3144 hysterectomies, 6 of these discovered at autopsy; Herman (1946), 4 in 7966 gynecologic operations. Instances of ureteral injury have been collected by Sampson (1902), 38; Barney (1912), 30; Peterson (1920), 72; Herman (1923), 28 bilateral; Bland (1925), 360 unilateral, 81 bilateral; Feiner (1936), 601 unilateral, 109 bilateral; Adams (1943), 782; Moore (1948) 800. There are probably many more such accidents, unreported or entirely unsuspected. Ligation of one ureter may result in silent death of the kidney.

The primary operations complicated by accidental ureteral injuries are, in order of frequency, radical hysterectomy, abdominal complete hysterectomy, supracervical hysterectomy, vaginal hysterectomy, salpingo-oophorectomy for chronic inflammatory lesions, anterior colporrhaphy, radical operation for carcinoma of the rectum and rectosigmoid. The types of injury reported have been ligation, division, partial excision, crushing by clamp, partial ligation by perforation with needle, kinking by ligature, laceration, necrosis secondary to contusion or denudation. Unilateral injury is about 6 times as frequent as bilateral injury.

The earlier contributors to the subject were general surgeons and gynecologists. Some of them, Kelly for example, were keenly interested in urology. They were concerned chiefly with the management of section or partial excision discovered at the primary procedure and with the technics for immediate repair. As more extensive and radical pelvic surgery was done for complex lesions distorting the anatomy, and as efforts to control hemorrhage by clamp, ligature, or suture increased the chances for compromising one or both ureters, their injury was usually not recognized at the primary procedure. The postoperative manifestations and the sequelae brought the earlier cystoscopists and later the urologists to the aid of the gynecologists and intestinal surgeons.

Thus, with few exceptions, the contributions of the past 30 years have come from urologists. The responsibility for the prevention of these accidents and their prompt recognition, however, rests squarely with the gynecologist or sur-

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Read at annual meeting, American Urological Association, Atlantic City, N. J., June 24, 1952.

geon who performs the primary operation. It is also his responsibility to call in expert aid when he merely suspects that a ureter has been compromised because the life of a kidney and often the life of the patient are at stake. The impression may be generally abroad that these accidents occur in the hands of tyros or occasional operators. If I were to divulge the names of the gynecologists and surgeons in whose hands the primary accidents occurred in the 15 patients herewith reported (in whom injuries to ureter, bladder, or both occurred), you would be convinced to the contrary. They were on staffs of accredited hospitals, not a few were heads of service, some held teaching positions.

TABLE 1. *Procedures for accidental section of one ureter discovered at primary operation*

A. Uretero-ureterostomy
  1. End to end transverse: Tauffer, 1885 (published 1891); Schopf, 1886
     End to end oblique: Bovee, 1897
  2. Upper end invaginated into lower end: Poggi, 1887, modified by Boari; Peterson, R., 1920
  3. Upper end to side of ligated lower end
  4. Upper end invaginated into side of ligated lower end: Van Hook, 1893; H. Kelly, 1894; McEachern, 1921
  5. Side to side, both ends being ligated: Monari, 1895
  6. End to end *over catheter* (size 10 to 13): Albarran; Young*
  7. End to end with drainage of kidney pelvis and splinting of ureter, thru side of upper segment*: McArthur, 1925; Bump and Crowe, 1929; Curtis, 1929

B. Ureterocystostomy*
C. Transuretero-ureterostomy (with or without catheter)*: Sharpe, 1906; Higgins, 1935; Neuswanger, 1936; Moore, 1918; Davis and Leroy, 1950
D. Ureterocutaneous fistulization: not desirable
   Ureterovaginal fistulization: not desirable
E. Uretero-intestinal anastomosis: (should be avoided)*
F. Ureteral ligation: Curtis, 1929; (should be avoided)

* Selectively applicable at secondary operation for sequelae of other types of injuries.

TABLE 2. *Techniques of uretero-cystostomy (first by Tauffer, 1877) (ureterovesical implantation, ureterovesical neostomy)*

1. Direct, end to side suture: Krug, Boldy (accredited by Albarran)
2. Direct implantation, end into side; end of ureter split, flaps sutured to bladder wall from within: Sampson, 1905; Albarran, Burns, 1928
3. Direct implantation, end free in bladder; sutures of ureter to bladder, outer coats only: Furniss, 1918; Young
4. Oblique implantation, end into side; with inlying catheter; using intramural ureter and catheter: Witzel, 1896; Dodson, 1946; Patton, 1939
5. Ureter into tube from bladder flap: Casati and Boari, 1904; Ockerblad, 1936
6. Vaginal route: Mackenrodt's "entropionizing" (accredited by Kelly)
7. Combined vaginal and vesical route: Finlay, 1938

These patients all came under my observation and treatment. I have seen at least as many on ward services and in consultation. I know of three instances in which the left ureter was cut during resection of the left colon in the past 2 years. As Beach said, "surgical injury to the pelvic ureter is all too common, often not reported, may go unrecognized and in most cases preventable".

The experience of Sisk at the Wisconsin General Hospital emphasized the effectiveness of preoperative introduction of inlying catheters in the prevention of these accidents. This was routine for many years in "difficult" pelvic operations. Only one ureter was injured but in this single instance catheters had not been introduced. It would appear that no surgeon can predict when a "simple" operation may become "difficult" at some stage of the dissection. Ureteral catheters should therefore be passed in every case before pelvic surgery is undertaken. It is the best prophylaxis against ureteral injury.

TABLE 3. *Sequelae of ligation of one ureter*

- Post hydronephrotic atrophy
  - a. Aseptic (often silent)
  - b. With subsequent infection
- Necrosis and extravasation
  - a. Intraperitoneal
  - b. Extraperitoneal
- Fistula direct, or indirect (per abscess cavity or sinus tract)
  - a Vaginal
  - b. Abdominal
- Secondary contracture of stoma or fistulous tract with resultant hydro-ureteronephrosis and
  - a. Atrophy (may be silent)
  - b. Recurring pyelonephritis, may necessitate nephrectomy
  - c. Pyo-ureteronephrosis, necessitates nephrectomy
- Azotemia if other kidney is deficient "reflex suppression?"

TABLE 4. *Analysis of 15 cases presented in this paper*

Unilateral ureteral injury	11
Bilateral ureteral injury	2
Vesicovaginal fistula*	2
Vesicocervical fistula	1
Primary causative operation	
Abdominal complete hysterectomy	6
Abdominal supracervical hysterectomy	3
Myomectomy (intraligamentous)	1
Anterior colporrhaphy	3
Salpingo-oophorectomy	1
Cesarean section	1

* In one case both ureteral injury and vesicovaginal fistula.

Tables 1 and 2 contain the procedures which have been used for immediate repair and secondary correction of unilateral ureteral injury. Table 3 lists the sequelae of ligation of one ureter.

In tables 4 and 5 are presented the data on 15 cases (13 ureteral, 2 vesical) which have been under my own observation. There were no deaths. Three kidneys had to be sacrificed: two in 11 unilateral injuries; one in the two instances of bilateral injury and in the second one kidney died in situ. Thus in 13 cases of ureteral injury (15 ureters injured), four kidneys were lost, about 25 per cent. Of 8 ureterocystostomies performed, 6 were successful. One failed and the kidney had to be removed, another was followed by renal infection ultimately requiring nephrectomy. This procedure therefore gave satisfactory outcome in 6 of 8 instances, 75 per cent.

TABLE 5. *Resultant lesions in 18 ureteral injuries*

Stricture	3
Occlusion	3
Ureterovaginal fistula	2
Ureterocervical fistula..	1
Uretero-abdominal and vaginal fistula	2
Retroperitoneal extravasation and fistula	2

Procedures in 11 unilateral injuries

Nephrectomy unavoidable		2 recovered
Nephrectomy after failure of ureterocystostomy		1 recovered
Reconstruction over inlying catheter		1 well
Resection and anastomosis end to end over inlying catheter		1 improved
Ureteral cystoscopic dilation		1 improved
Ureterocystostomy		5 successful
Preceded by nephrostomy	1	
Preceded by pyelostomy	1	

EFFECT OF TEMPORARY CLAMPING OF THE URETER

Sampson reported in 1902 four instances from Kelly's service in which a clamp had been applied to a ureter and was released. In three, curiously, a ureteral catheter was in situ and the crush broke the catheter. In one instance the upper fragment of the catheter was not removed, the patient died. In two it was removed and altho one patient developed a temporary urinary fistula, both patients recovered. In the fourth the accident occurred in doing a nephropexy, there were no after effects.

Furniss in 1918 reported two instances in which he had freed a ureter for about 3 cm., inadvertantly left a clamp on it for 7 or 8 minutes. In one ureterovaginal fistula developed on the eighth day, in the other on the twentieth day.

Maury in 1923 noted a clamp had been applied to a ureter; it was promptly released and there were no sequelae. There was, however, no checkup by x-ray or cystoscopy.

In case 3 here reported a clamp applied and removed resulted in delayed necrosis and extravasation.

It seems to me that the procedure should be immediate cystoscopy, introduction of a ureteral catheter, leaving it in place for three weeks as protection against fistula.

LATE RESULTS

Some reports of late results following various procedures employed in the management of ureteral injury warrant notice. The following are cases in which immediate uretero-ureteral anastomosis was performed. Frederick did one in 1901; the patient was well in 1906, but at autopsy in 1910 he found stenosis at the site of union with hydro-ureteronephrosis above it (quoted by Bump and

Crowe). McEachern, using a modified Van Hook procedure in 1919, found a normally functioning kidney and obtained a normal pyelo-ureterogram in 1926. Delayed anastomosis of the end of the injured ureter into a tube constructed from a bladder flap was performed by Ockerblad in 1936, who obtained a normal pyelo-ureterogram in 1946. Caughlan employing the same technique in 1941 reported good function and regressing hydronephrosis 5 years later, 1946.

In cases of ureterocystostomy, H. Dawson Furniss, using his simple method for free direct implantation, in 1919 had the opportunity to check the result 12 years later, 1930. Although the patient had marked hypertension, blood pressure 250/150, the implanted ureter was catheterized and a normal pyelo-ureterogram was demonstrated. Beer in 1933 was able to follow up 12 patients in whom ureterocystostomy was done for various primary procedures. Eight were well, four had evidences of renal infection. In eight, immediate excretory urography showed good results but after several years only five remained so. Cystograms in four showed no reflux. Dodson reported excellent results as indicated by excretion urography in two cases of ureterocystostomy using the catheter splint method, 12 and 15 months later. The cases of Patton and Hess in which the ureter was transplanted through the intramural lower segment showed normal pyelo-ureterograms 6 and 5 months thereafter, respectively. In Moore's 2 cases of ureterocystostomy normal excretory urography was found 7 and 27 months later, respectively.

In the newer procedure of transuretero-ureterostomy Higgins 1935 reported satisfactory function and contour of both kidneys on excretory urograms 1½ years after operation. Moore's case, 1948, in which the same procedure was used, also proved successful by excretion urography 7 months after the right ureter was implanted into the left, which had been previously implanted into the bladder. He also reported a case of transuretero-pyelostomy with good urographic result 8 months after operation. The patient of Davis and Lee (1950) had the wrong kidney removed in an attempt elsewhere to cure a ureterovaginal fistula. They anastomosed the dilated left ureter to the side of the right ureter which fortunately had been left in situ when the wrong kidney had been removed. Excretion urography at 6 months showed good union and regressing pyelectasis.

As to late results in the cases reported in this paper, uretero cystostomy was proven satisfactory by excretion urography 5 months, 20 months and 5 years after operation (cases 2, 11, 12). Reconstruction of ureter was checked by cystoscopy 4 years later (case 3). Resection of strictured ureter with end to end anastomosis was satisfactory at 6 months (case 7).

BILATERAL URETERAL OBSTRUCTION

This is the gravest of surgical accidents in pelvic surgery. There has been sharp divergence of opinion as to the best management for the patient who is found to be anuric shortly after the primary operation. In 1915 Caulk performed bilateral nephrostomy for a patient in uremia due to such occlusion on the eighth day. Nothing else was done. The patient voided on the fifty-eighth day and on the sixty-eighth day, the nephrostomy tubes having been removed, all urine was passed per *vias naturales*. Five years later renal function was within normal limits. This appears to be a unique experience. Experimentally Caulk and Fischer demonstrated that in dogs No. 2 plain catgut ligatures were never absorbed in less than 3 weeks. At 5 weeks the occluded ureters gave first evidence of opening up, at 6 weeks a channel was established and from 8 to 12 weeks there was progressive improvement in drainage. At 1 year a drained kidney had recovered almost completely whereas an undrained kidney had undergone complete atrophy.

They concluded that nephrostomy must be done within 2 weeks after the time of unilateral occlusion if these results are to be attained. Deligation is a difficult and hazardous procedure. It may result in secondary hemorrhage on releasing the ligature. It often results in ureteral fistula necessitating ureterocystostomy. Nephrostomy is by far preferable.

Herman, on the other hand, in 1923 championed the cause of abdominal deligation with the simultaneous aid of cystoscopy and ureteral catheters. The latter impinging against the points of obstruction, acted firstly as a guide to the location of the offending ligatures. Once these were removed, the catheters were passed to the renal pelvis and were left in situ secondly for drainage and healing of the compromised ureters. He opened the ureters above the level of the obstruction and probed downward into the bladder to demonstrate patency below. In his patient operated upon by this method 48 hours after supracervical hysterectomy the blood urea nitrogen was 32 mg., both ureters were obstructed at 5 cm. and were found at operation considerably dilated. On the right side probing demonstrated a second offending ligature below the first which had been removed. This was also removed. The patient made a good recovery and 3 months later No. 6 catheters were passed and no retention was found in the renal pelves.

Barney reported a mortality of 33.3 per cent in 16 bilateral ureteral occlusions as against 17.8 per cent in 46 unilateral injuries. Herman had collected 28 bilateral cases by 1923, with an approximate 30 per cent mortality. Of 10 instances of bilateral nephrostomy, 5 died (50 per cent) only 2 had complete recovery (20 per cent). Smith performed bilateral ureterocystostomy secondarily in these two. Of 8 deligations, 2 died (25 per cent) and 6 recovered (75 per cent). On the basis of these collected figures and his one favorable experience with deligation, Herman concluded that this was the preferable procedure as opposed to nephrostomy.

Feiner in 1938, however, collected 12 cases of bilateral ligation. In 5 bilateral nephrostomy was done: 2 had subsequent end to end uretero-ureterostomy, in 1 a secondary nephrectomy was necessary, in another both ureters were transplanted into the sigmoid, 1 died. Thus there was 20 per cent mortality. In 6 cases deligation was done; in 1 case, at the 48 hours, patient recovered but one kidney had to be removed; 5 patients died on the third and fourth days, 83 per cent mortality. The twelfth patient in whom no surgery was undertaken died on the fourth day. Feiner then presents his own experience with 4 cases of bilateral ligation: in 2, abdominal deligation was done, both died; in 1, after colporrhaphy, vaginal deligation was successful; in the fourth right nephrostomy was done. On the twenty-fourth day cystoscopy showed good efflux of indigo carmine in 5 minutes on both sides but catheters were obstructed at 5 cm. on both sides. The blood urea nitrogen was 110 mg. on the second day, 76 mg. on the fourth day, 17 mg. on the eighth day. No follow up in this case was reported, so that ultimate outcome is problematical.

Feiner concluded, firstly, that nephrostomy is the safer and preferable procedure. *In making one's decision the operator, secondly, should keep in mind* ultimate preservation of both renal and ureteral function.

In 1943 Adams collected 17 cases of bilateral ligation. In 6 deligations, 1 failed, 5 died. In 8 nephrostomy or ureterostomy was performed, 7 were cured, only 1 died. The secondary procedures in this group consisted of 2 ureters implanted into bowel, 4 spontaneous cures, 1 nephrectomy.

If these two series collected by Feiner and by Adams are combined we have *12 deligations with 10 deaths (83 per cent), 13 nephrostomies* with 3 deaths (23 per cent), in 3 additional untreated cases the patients also died.

Moore commented on the wide divergence of opinion expressed by writers on the subject of deligation quoting Hepler's statement that the mortality was 90 per cent. His own preference seems to be for nephrostomy or ureterostomy as an emergency measure followed by deligation, cystoscopic dilatation, ureterocystostomy etc. as indicated in various situations.

It seems to me that the weight of evidence is against attempting deligation as the first attack upon bilateral ureteral obstruction following pelvic surgery. It is a difficult operation, it carries a prohibitive mortality rate, it is unnecessary. Nephrostomy (or ureterostomy) preferably bilateral, is a much simpler and much more effective procedure. It permits of managing the ureteral obstruction subsequently according to the requirements of the individual patient with the objectives being the saving of both kidneys, and the restoration of ureteral drainage into the urinary bladder.

TECHNIQUE OF URETEROCYSTOSTOMY

The method herewith described is that used in the first case in 1937, and subsequently *modified.* A No. 16 Foley catheter with 5 cc bag is introduced per urethram into the bladder, and the latter distended with 6 to 8 ounces of sterile saline. Through a pararectus incision the rectus muscle is retracted medially. The affected ureter is exposed extraperitoneally as it crosses the iliac vessels. It is followed down to the point of obstruction, transected and freed with its sheath for 3 or 4 cm. The distal end need not be disturbed, as it has been closed off by the accidental injury during the primary operation. A red rubber catheter of appropriate caliber (No. 10 to 18) is prepared by cutting off the tip and eye obliquely and making a few side holes near this end. It is introduced upward into the ureter for about 10 or 12 cm. The cut end of the ureter is stitched to the catheter with three fine chromicized catgut sutures. A few side holes are made in the catheter just below this point, through which all urine will be drained from the bladder.

The latter is now exposed at an appropriate level on the affected side, the water is let out by way of the Foley catheter. Using a No. 11 blade a small oblique incision is made through the muscularis and then the muscosa. The tip of the Foley catheter is now grasped, the bag is deflated and the tip is brought out of the incision in the bladder wall. The end of the ureteral splint catheter is stitched to the tip of the Foley catheter. An assistant gently pulls out the latter with the splint following until about a centimeter of the ureter is within the bladder. Three fine chromic catgut sutures now attach the ureter to the muscular coats of the bladder. The muscularis of the latter is closed over the splinted ureter, thus making a valve-like implantation. A Penrose drain is placed down to this site and the wound is closed. The ureteral catheter splint which will now drain both the kidney and the bladder is fixed by suture to a labium minus. The method is that which Dodson described in 1946.

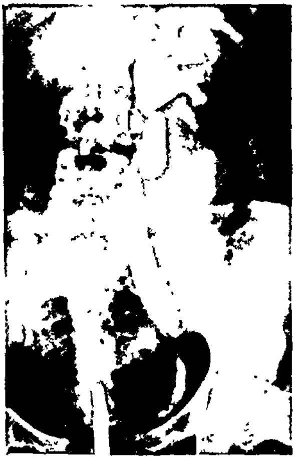

FIG. 1. Case 7.—Left retrograde pyelo-ureterogram. Stricture of left ureter discovered 18 years after supracervical hysterectomy.

AUTHOR'S CASES OF UNILATERAL INJURY

Case 1. November 5, 1937, L. P. aged 40. Abdominal complete hysterectomy. Left uretero-abdominal, then left ureterovaginal fistula. Ureterocystostomy; failure. Left nephrectomy.

Case 2. May 16, 1938, S. L. aged 36. Abdominal supracervical hysterectomy. Left ureterocervical fistula. Ureterocystostomy. Successful.

Case 3. June 22, 1944, J. G. aged 34, obese. Abdominal myomectomy for right intraligamentous fibromyoma arising from cervix. Clamp on right ureter, removed. Postoperative partial necrosis of ureter, pelvic urinary extravasation, and abdominal urinary fistula. Reconstruction of right ureter over inlying catheter. Cured.

Case 4. January 18, 1944, M. O. aged 41. Abdominal complete hysterectomy. Urine from vagina a week later. Some vaginal procedure failed, then some abdominal procedure after which, abdominal urinary fistula. Left uretero-abdominal fistula. Vesicovaginal fistula. Left nephrectomy. Successful repair of vesicovaginal fistula.

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Case 5. November 7, 1946, G. G. aged 35. Supracervical hysterectomy, fibroids, intraligamentous cysts, endometriosis. Right ureterovaginal fistula. Right ureterocystostomy. Successful.

Case 6. December 31, 1947, H. K. aged 39. Abdominal complete hysterectomy for endometriosis. Left ureterovaginal fistula which closed spontaneously followed by stricture of left ureter. Treated by cystoscopic dilatation. Improved.

Case 7. July 25, 1946, T. R. aged 53. Abdominal supracervical hysterectomy 18 years ago. Stricture of left ureter with dilatation of ureter (fig. 1), hypertension. Excision of strictured area, end to end anastomosis over inlying catheter. Successful.

FIG. 2. Case 9.—Right pyelo-ureterogram by way of nephrostomy tube. Status after nephrostomy and subsequent ureterocystostomy. Ureteral catheter splint in situ.

Case 8. May 23, 1948, M. S. aged 38. Abdominal complete hysterectomy. Left retroperitoneal extravasation, incision and drainage, urinary fistula. Nephrectomy.

Case 9. September 24, 1951, S. L. aged 43. Abdominal complete hysterectomy. Right ureter ligated. Nephrostomy. See figure 2. Subsequent right ureterocystostomy. Successful.

Case 10. June 29, 1940, R. L. aged 52. Anterior colporrhaphy. Right ureterovaginal fistula. Right ureterocystostomy. Successful.

Case 11. December 2, 1944, E. H. aged 54. Manchester (Fothergill) operation for descensus uteri. Right ureter ligated. Right lumbar ureterostomy. Subsequent right ureterocystostomy. Successful.

AUTHOR'S CASES OF BILATERAL URETERAL INJURY

Case 12. July 15, 1946, C. L. aged 33. Anterior colporrhaphy. Bilateral ureteral occlusion. Surgeon attempted vaginal deligation, failed on right, caused ureterovaginal fistula on left. Right nephrostomy. Left ureterocystostomy. Successful.

Right ureterocystostomy. Right nephrostomy tube removed. Bladder neck obstruction, for which transurethral resection was done, but it had to be repeated to establish complete emptying of bladder. Vesicovaginal fistula following this procedure repaired. See figure 3.

Recurring episodes of right renal infection necessitated nephro-ureterectomy. Subsequent episodes of left renal infection due to reflux controlled by chloromycetin.

Case 13. February 1, 1939, M. C. aged 42. Abdominal complete hysterectomy. Bilateral ureteral occlusion. Bilateral nephrostomy maintained for 3 months. Healed after removal of tubes. Ureterovaginal fistula thereafter for 2 months (probably left). Healed. Hematuria, painless 13 years later. Status 18 years later: left ureter occluded, left kidney dead. Right ureteral stricture at 3 cm, small stone in lower pole of right kidney; right renal hematuria due to stricture. See figure 4.

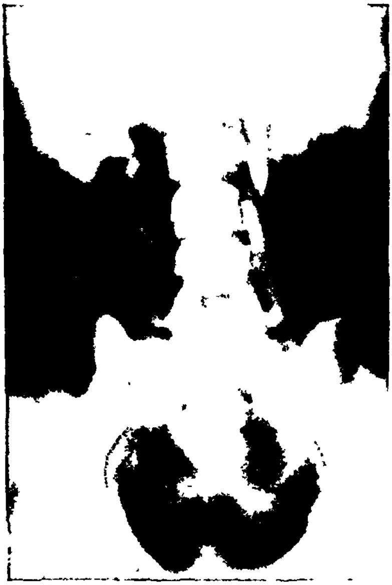

FIG. 3. Case 12.—Excretory urogram, laminogram, 20 minutes. Six weeks after second ureterocystostomy (right). Both ureters have been successfully implanted into bladder.

AUTHOR'S CASES OF VESICAL FISTULA

Case 14. November 17, 1939, C. K. aged 27, divorced, married at 16 years. Bilateral salpingectomy, partial oophorectomy. Thereafter frequent voiding and "dribbling of urine." Vesicovaginal fistula undiscovered for 4 years. Three attempts to repair vaginally failed.

Case 4. (Which see.) Patient had sustained both vesicovaginal fistula and left ureteral injury during abdominal complete hysterectomy. Repaired vaginally successfully.

Case 15. September 21, 1937, M. S. aged 41. Cesarean section 22 years ago. Undiscovered vesicocervical fistula. Repaired by abdominal route. Wound dehiscence. Subsequent repair of incisional hernia. Cured.

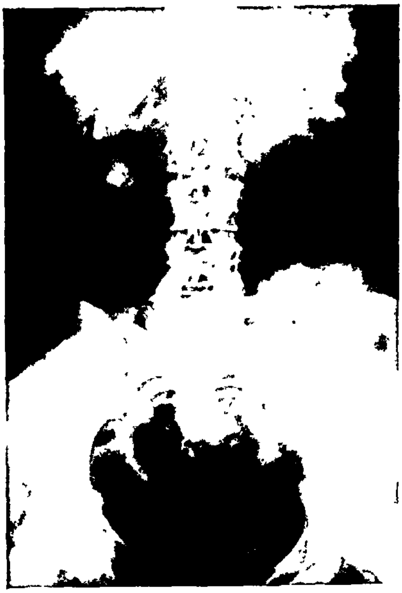

FIG. 4. Case 13.—Excretory urogram, 40 minutes. Eighteen years after bilateral nephrostomy for bilateral occlusion following abdominal complete hysterectomy. Completely occluded nonfunctioning left kidney. Hematuria due to stricture of right lower ureter. Small calculus in lowermost minor calyx.

CONCLUSIONS

It is highly advisable for gynecologists and surgeons to have a urologic survey made in every patient in whom pelvic or vaginal surgery is contemplated. This implies excretory urography which may disclose unsuspected anomalies, malpositions, dilatations, etc. If the information thus derived is inadequate or inconclusive, cystoscopic and retrograde study may be needed.

The introduction of inlying catheters into the ureters by way of the cystoscope immediately before pelvic surgery has been urged time and again by some gynecologists and some urologists. They may well be left in for 24 hours. This precaution will undoubtedly safeguard the patient, and protect the operator from untoward accident. It will also fortify his medico-legal position in the event that an incident occurs, a situation unlikely to arise with this precaution taken.

If injury to a ureter occurs and is observed during operation, immediate repair by uretero-ureterostomy or ureterocystostomy, preferably with an inlying catheter splint, should be done. Ligation of the injured ureter should be abandoned, even when it is known that the other side is completely normal. It spells sure death and destruction of one kidney, and may lead to sequelae requiring subsequent nephrectomy. Temporary external drainage is preferable (ureterostomy through lateral incision in the ureter) in an emergency situation.

If after pelvic surgery persistent distention, flank pain and/or ureteral pain appear the possibility of unilateral ureteral injury should always be in mind. An excretory urogram, circumstances permitting, or cystoscopic observation with indigo carmine intravenously (chromoscopy) will settle the issue.

If unilateral impairment is detected early, nephrostomy, pyelostomy, or ureterostomy is the procedure of choice. I prefer nephrostomy. If not detected early there may be silent death of the kidney. Otherwise extravasation, urinary fistula by way of the vagina or abdominal wound will give the kidney temporary relief and supply obvious evidence to the surgeon of what has taken place. The sooner direct urinary drainage is established the better. In rare instances this may be accomplished fortunately with the cystoscope and ureteral catheter.

If a ureterovaginal, ureterocervical or uretero-abdominal fistula ceases to drain urine, do not be lulled into a false sense of relief. It may spell the death of the kidney. It may be followed by the clinical manifestations of pyelonephritis or pyo-ureteronephrosis. This may vitiate one's chances to save the kidney even by nephrostomy, and certainly renders subsequent conservative procedures less likely to succeed despite the availability of potent antibiotics. Infection is the chief cause of our failures.

If soon after operation urinary output drops or ceases, never assume that it is due to "suppression" or "reflex anuria," have the ureters investigated at once by cystoscopy.

Bilateral obstruction being thus ascertained, it is my firm conviction (and others are in accord) that deligation should not be attempted. If the abdominal route was used, remember that you are dealing with a patient who has but recently undergone a lengthy procedure probably associated with blood loss and shock. The operation you contemplate is difficult and requires simultaneous cystoscopic assistance. If the original procedure was vaginal the deligation is no less difficult and one will necessarily destroy the pelvic floor repair in the attempt.

Nephrostomy, at least unilateral, preferably bilateral is the first choice. It is life saving. It permits subsequent flexibility of approach to the final solution of the problem. If in due time the offending catgut ligatures are absorbed one may, rarely, require only ureteral cystoscopic dilatation to save life and kidneys. Restoration of bilateral ureterovesical continuity may be established at leisure and in two stages.

Never omit the dye test for vesicovaginal fistula. It may be a difficult diagnosis to rule out. It may occur concomitantly with ureteral injury.

The operation of ureterocystostomy seems to be the best procedure for damage to the lower ureter. Oblique implantation with the free end of the damaged ureter projecting into the bladder lumen and a catheter splint for kidney drainage which I utilized as early as 1937 in the first case herewith reported (Dodson published the method 1946). The same catheter may be used for bladder drainage per urethram.

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THE CLINICAL EFFECT OF PITUITARY ADRENOCORTICOTROPHIC HORMONE IN THREE CASES OF SEVERE CHRONIC INTERSTITIAL CYSTITIS

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The treatment of chronic interstitial cystitis (Hunner's ulcer) with pituitary adrenocorticotrophic hormone (ACTH) was suggested by the work of Fister[1] in which the histologic similarity with lupus erythematosus was pointed out; and by the work of Elkinson, et al.[2], and Thorn[3] in which lupus erythematosus responded favorably to ACTH.

Three patients with severe and refractory forms of interstitial cystitis were selected for trial therapy. Each had had the disease at least ten years with a progression in symptoms in spite of occasional temporary remissions related to silver nitrate instillations, vesical dilations and fulgurations. Routine studies, including biopsy, had revealed no evidence of neoplasm, tuberculosis, syphilis, urinary obstruction or any disorder in the upper urinary tracts. Routine urine culture was sterile in two but a variety of organisms were grown from the urine of one patient. These 3 patients had failed to respond to vitamin E administration (dosage equivalent to 300 mg. of alpha tocopherol daily) after 3 to 4 months. The patients were also selected because of their willingness to cooperate, their good intelligence, and their freedom from systemic disease that would contraindicate the employment of ACTH or complicate the interpretation of the results obtained in this study.

An observation period was utilized for pretreatment clinical and laboratory studies which included cystoscopy, measurement of the bladder capacity, urine culture, routine blood and urine examinations, excretory urograms, Mazzini test for syphilis, basal metabolic rate determination, roentgenography of the chest, and serum glucose, uric acid, albumin, globulin, sodium and potassium levels. Frequency of urination, nocturia and the quantity of voided urine for each micturition were recorded.

The pituitary adrenocorticotrophic hormone* was administered to each patient intramuscularly in daily determined portions divided into four doses. During the treatment normal saline was substituted for ACTH as the daily alloted amount of hormone was decreased. In the control studies normal saline

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Read in part before the 2nd Gerontological Congress, St Louis, Mo

Read at annual meeting, American Urological Association, Atlantic City, N J June 24, 1952

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* Supplied with the co-operation of Dr John R Mote of Armour and Company

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THE CLINICAL EFFECT OF PITUITARY ADRENOCORTICOTROPHIC HORMONE IN THREE CASES OF SEVERE CHRONIC INTERSTITIAL CYSTITIS

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The treatment of chronic interstitial cystitis (Hunner's ulcer) with pituitary adrenocorticotrophic hormone (ACTH) was suggested by the work of Fister[1] in which the histologic similarity with lupus erythematosus was pointed out; and by the work of Elkinson, et al.[2], and Thorn[3] in which lupus erythematosus responded favorably to ACTH.

Three patients with severe and refractory forms of interstitial cystitis were selected for trial therapy. Each had had the disease at least ten years with a progression in symptoms in spite of occasional temporary remissions related to silver nitrate instillations, vesical dilations and fulgurations. Routine studies, including biopsy, had revealed no evidence of neoplasm, tuberculosis, syphilis, urinary obstruction or any disorder in the upper urinary tracts. Routine urine culture was sterile in two but a variety of organisms were grown from the urine of one patient. These 3 patients had failed to respond to vitamin E administration (dosage equivalent to 300 mg. of alpha tocopherol daily) after 3 to 4 months. The patients were also selected because of their willingness to cooperate, their good intelligence, and their freedom from systemic disease that would contraindicate the employment of ACTH or complicate the interpretation of the results obtained in this study.

An observation period was utilized for pretreatment clinical and laboratory studies which included cystoscopy, measurement of the bladder capacity, urine culture, routine blood and urine examinations, excretory urograms, Mazzini test for syphilis, basal metabolic rate determination, roentgenography of the chest, and serum glucose, uric acid, albumin, globulin, sodium and potassium levels. Frequency of urination, nocturia and the quantity of voided urine for each micturition were recorded.

The pituitary adrenocorticotrophic hormone* was administered to each patient intramuscularly in daily determined portions divided into four doses. During the treatment normal saline was substituted for ACTH as the daily alloted amount of hormone was decreased. In the control studies normal saline

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Read at annual meeting, American Urological Association, Atlantic City, N. J. June 24, 1952.

[1] Fister, G. M.: Similarity of interstitial cystitis (Hunner's ulcer) to lupus erythematosus. J. Urol., 40: 37, 1938.

[2] Elkinton, J. R., Hunt, A. D., Godfrey, L., McCrory, W., Rogerson, A., and Stokes, J.: Effects of ACTH in patients with collagen and allied diseases. Proc. First ACTH Conference, pp. 429–437. Philadelphia: The Blakiston Co., 1950.

[3] Thorn, G. W., Bayles, T. B., Massell, B. F., Forsham, P. H., Hill, S. R., Smith, S., Jr., III and Warren, J. E.: Studies on the relation of pituitary-adrenal function to rheumatic disease. New Eng. J. Med., 241: 14, 1949.

* Supplied with the co-operation of Dr. John R. Mote of Armour and Company.

alone was used. ADACTAR, a special medium in which ACTH can be mixed for intramuscular injection and which permits slow absorption within a 24 hour period, was used in the determination of the minimal maintenance dosage in 2 cases. The laboratory measurements were repeated at intervals during the study. In addition the patient's blood pressure, weight, fluid intake and urine output were measured daily.

Sodium pentobarbital gm. 0.1 was given at times during the night if the patients complained sufficiently of inability to sleep, and in one instance Floraquin was used for mild trichomonas vaginitis. Otherwise, all sedation, local, parenteral and oral medications were denied the patients.

The observations which proved to be reliable criteria of improvement were the increase in the measured bladder capacity, the diminution of pain, and the cystoscopic disappearance of the bladder lesions. The bladder capacity was measured by instillation of saline into the bladder to the point of onset of pain or the sensation of bladder fullness. In the establishment of the criteria of improvement, we overlooked the obvious value of cystograms as a means of demonstrating the improvement in the bladder capacity. The subjective evaluation of pain was employed after the patients had been educated to interpret the degree of pain they perceived either before, during or after micturition on a scale which extended from 0, the absence of pain, to 10, the maximal pain of this kind experienced. It is of interest to note that the subjectively determined curve of pain paralleled closely the curve of the eosinophiles, and these two responses were the most sensitive indicators of improvement or relapse. The bladder lesions were observed repeatedly by cystoscopic examination during all phases of this study.

Frequency, nocturia and the average volume of micturition were not reliable criteria of improvement. The average volume of micturition is a value obtained by dividing the urinary output in any twelve hour period by the number of voidings during the same period. Only in case 3 did these seem to parallel other signs of improvement. Apparently frequency, nocturia, and the average volume of micturition are too readily affected by the patient's emotional state for it was found that by discouraging these patients the frequency-nocturia increased and the average volume of micturition diminished. The converse was true with encouragement and assurance. This is illustrated in table 1 which correlates the attitude of patient 3 with frequency and the average volume of micturition while receiving normal saline 1–2 cc 4 times a day for 19 days. Close questioning of each patient disclosed that they had suffered from enuresis as children until two were 11 years of age, and until one was 14 years old. In each case a history of marked frequency, urgency and nocturia associated with stress, anxiety, worry or fear was elicited.

CASE REPORTS

Case 1. A. P., N. Y. H. No. 537053, a 48 year old housewife, complained of frequency, urgency, nocturia, and discomfort in the lower right side of the abdomen when the bladder became distended. Although occasional remissions had occurred, these symptoms had been slowly progressive for 10 years and were always increased by nervousness and anxiety. She had had enuresis until 11 years of age. Menstruation seemed to increase her symptoms. Six years earlier an abdominal exploration had been done but no relief resulted.

The excretory urogram was normal. Acid fast bacilli could not be found by smear or culture of the urine. A routine urine culture was sterile and routine urinalysis was within normal limits. Urine sediment smears examined by the Papanicolaou technique revealed no neoplastic cells. Just above the left ureteral orifice a hemorrhagic area without ulceration was seen. The symptoms progressed

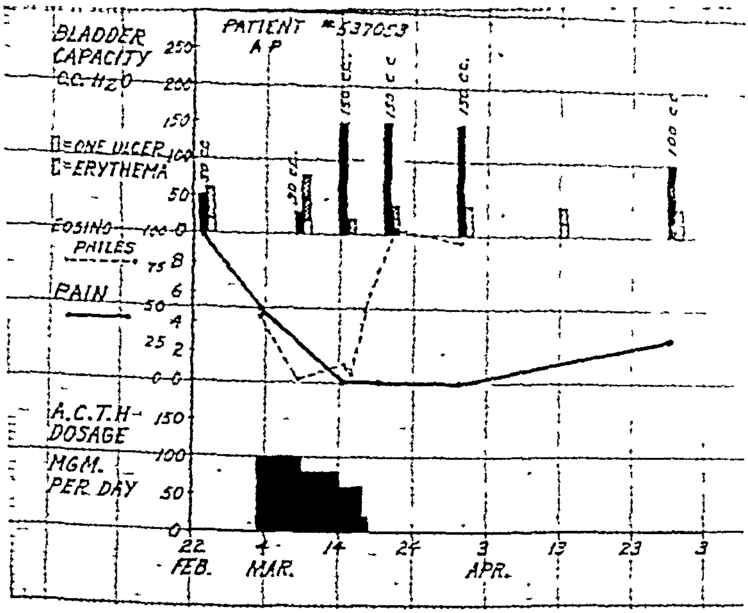

FIG 1

and 15 months later she was admitted to the hospital. At this time the vesical lesion was seen to be a typical Hunner's ulcer. A biopsy revealed chronic cystitis with fibrosis. A Frei test was negative. The previous pyelographic and urinary studies were repeated with the same normal results. The area of the ulcer was fulgurated and this provided marked relief for about 2 weeks. Vitamin E in daily doses equivalent to 300 mg. of alpha tocopherol was administered for 4 months without improvement. Fulguration was repeated after 6 months but again with only brief relief. The vesical capacity at this time was 70 cc, and the ulcer was easily identified.

The patient was then admitted to the hospital for a trial of therapy with ACTH (fig. 1). The urinary frequency was every 15 minutes in the day and every 30 minutes at night. The measured vesical capacity was 50 cc and the volume of individual voidings varied from 15 cc to 60 cc. A typical ulcer was seen in the dome. The patient received a total of 1160 mg of ACTH intramuscularly in divided doses during the 14-day treatment period. The measured vesical ca-alone was used. ADACTAR, a special medium in which ACTH can be mixed for intramuscular injection and which permits slow absorption within a 24 hour period, was used in the determination of the minimal maintenance dosage in 2 cases. The laboratory measurements were repeated at intervals during the study. In addition the patient's blood pressure, weight, fluid intake and urine output were measured daily.

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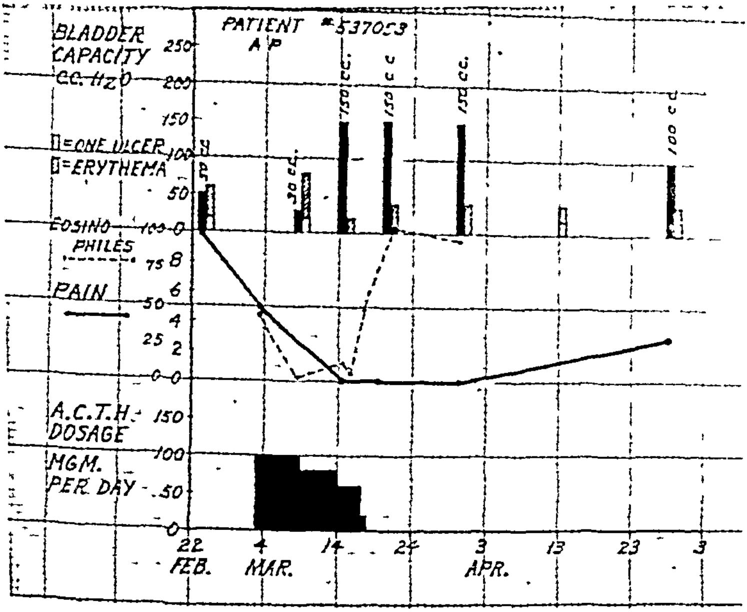

Fig 1

The patient was then admitted to the hospital for a trial of therapy with ACTH (fig 1). The urinary frequency was every 15 minutes in the day and every 30 minutes at night. The measured vesical capacity was 50 cc and the volume of individual voidings varied from 15 cc to 60 cc A typical ulcer was seen in the dome. The patient received a total of 1160 mg. of ACTH intramuscularly in divided doses during the 14-day treatment period. The measured vesical capacity increased to 150 cc and the ulcer could not be demonstrated at the end of 12 days. Pain disappeared within 10 days and the day frequency was reduced to 7 times in 12 hours. The nocturia, however, changed very little. After the cessation of treatment the ulcer reappeared in 12 days. The pain slowly returned to maximal intensity, and the measured capacity was 100 cc in 40 days.

Hysterectomy with bilateral salpingo-oophorectomy was carried out for chronic inflammatory disease, but without effect on the urinary tract.

Seven months after the first ACTH therapy, another trial was made (4320 mg. in divided doses during 96 days). Pain disappeared in 7 days and the ulcer could not be identified in 4 days. The measured vesical capacity increased from 110 cc to 230 cc in 28 days (fig. 2).

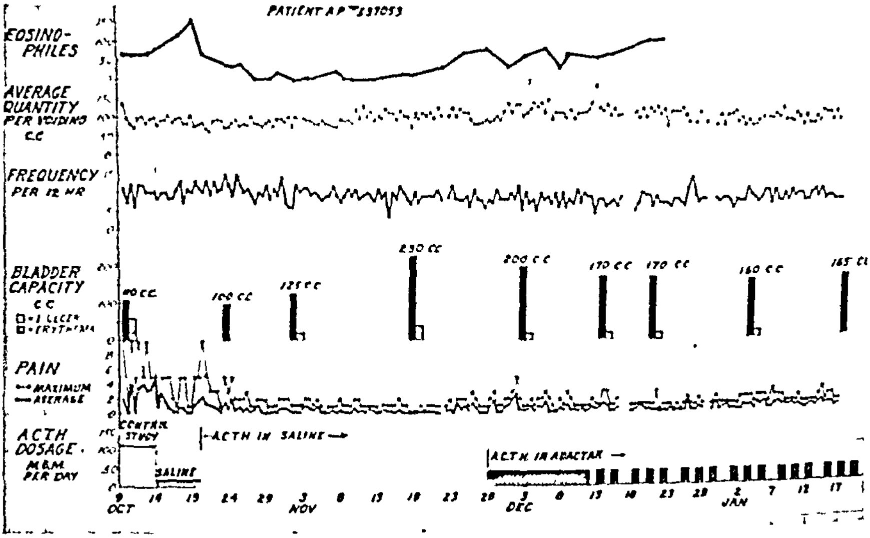

Fig. 2

An attempt was made to maintain this situation by intramuscular injection of 40 mg. of ACTH in 2 cc of Adactar 3 times a week. For 2 months this seemed satisfactory but the patient failed to appear for injections on two occasions, and the pain returned. Treatment was then discontinued.

This study seemed to demonstrate that ACTH might beneficially affect patients with advanced chronic interstitial cystitis. No local therapy to the bladder was given during the test period. Hormonal potency was determined by the eosinophilic response. The previous trial with vitamin E provided a partial control study regarding the effect of simple suggestion, but it was still quite possible that the general euphoria associated with ACTH therapy had been the main factor in her improvement. Interestingly the capacity of the bladder not only increased but did not return to its previous low when therapy was stopped. Maintenance dosage was successful until treatment was interrupted by the patient's failure to report on two occasions for treatment.

Case 2. O. N., N. Y. H. No. 525587, a 40 year old housewife, complained of frequency, urgency, nocturia, and hematuria for 13 years. The progress of these symptoms was slow and varied by remissions and exacerbations. However, during a recent pregnancy all symptoms disappeared until shortly after delivery. She was also definite that the symptoms were less during menstruation. Severe pain on vesical distention and the repeated appearance of gross hematuria were outstanding features in this case.

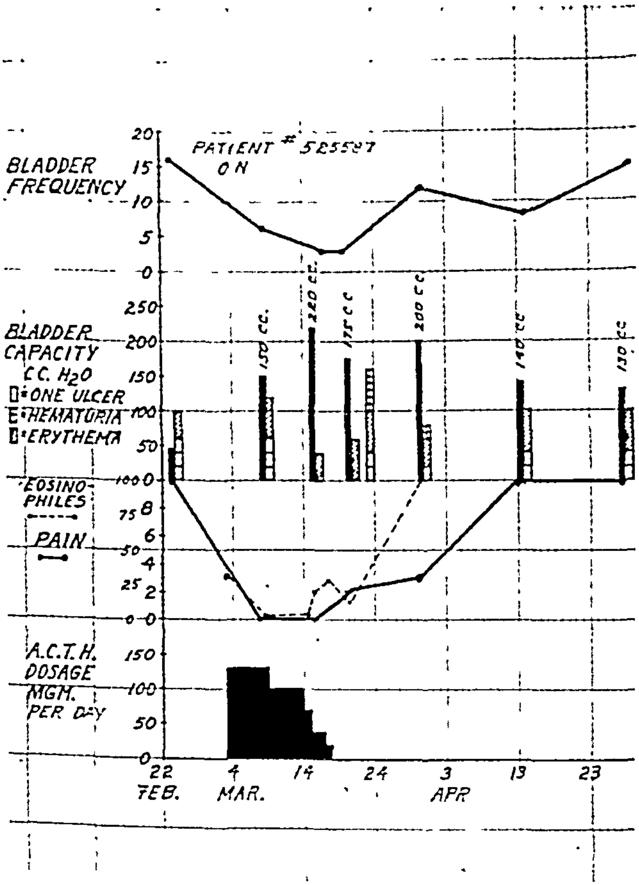

Fig. 3

Routine urinalysis was normal. Culture of the urine was sterile and acid fast bacilli were not found in smears or culture. Examination of the urine sediment by the Papanicolaou technique disclosed no neoplastic cells. Excretory urography was normal. A typical Hunner's ulcer was seen by cystoscopic examination, and a biopsy revealed chronic inflammatory changes. The lesion was fulgurated with relief for one month. Vitamin E in daily doses equivalent to 300 mg. of alpha tocopherol was taken for 3 months even though the patient thought this aggravated her symptoms. Two and 4 months after the fulguration the ulcer was easily visualized.

The patient was then admitted for trial of ACTH therapy (fig. 3). The pain was the maximal ever experienced and the measured bladder capacity was 45 cc. The left side of the bladder was erythematous and showed three separate Hunner's ulcers near the dome. A total of 1160 mg of ACTH was given intramuscularly in divided doses during 14 days. All pain disappeared in 5 days. At 12 days the measured capacity was 220 cc and the ulcers could not be demonstrated. After the cessation of ACTH therapy, the ulcers reappeared in 5 days, the pain fully recurred in 26 days, and the measured bladder capacity had fallen to 130 cc after 40 days.

Eight months after the first therapy with ACTH she was readmitted to the hospital (fig. 4). The pain was maximal and cystoscopic examination revealed four ulcers. The measured bladder capacity was 150 cc. Normal saline (1 cc) was given intramuscularly 4 times a day for 17 days with the assurance that this was ACTH. The pain was not alleviated, the lesions remained unchanged, and the measured capacity actually fell to 100 cc. Without the patient's knowledge ACTH was substituted for the pure saline. The pain then disappeared in 5 days. The measured capacity was 185 cc and the ulcers were not demonstrable on the eighteenth day of ACTH administration. On a daily dose of 120 mg. edema, acne, and arthralgia appeared. When the dose was reduced to 80 mg. daily, these were alleviated but the vesical pain and ulcers reappeared. The dose was increased to 120 mg. daily again with relief of pain and disappearance of the ulcer but with a reappearance of edema, acne, and arthralgia. Maintenance was attempted with 80 mg and later with 120 mg. of ACTH in 2 cc of Adactar intramuscularly 3 times a week for 4 weeks. This was unsuccessful. The measured capacity diminished to 75 cc and the ulcers returned. The pain also returned but not to the maximal degree.

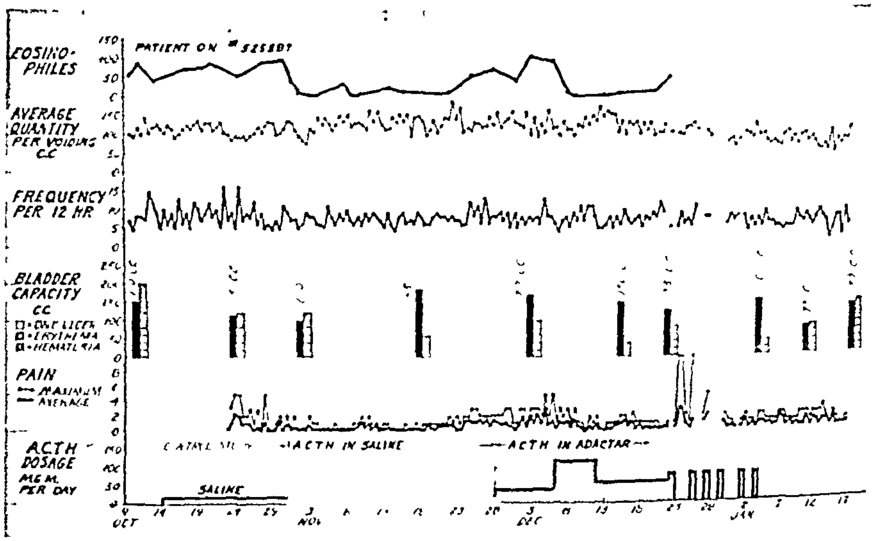

FIG. 4

This trial appeared to confirm the findings in the first case. The control period on saline injections and reassurance seemed to exclude simple suggestion as the principle cause of improvement, especially as her earlier experience with injections had been encouraging. Once more, however, maintenance therapy was unsuccessful. Indeed, even the intensive therapy had to be mildly toxic generally in order to obtain satisfactory vesical improvement.

Case 3. H. A., N. Y. H. No. 375252, a 48 year old housewife, complained of frequency, nocturia, urgency, suprapubic pain, and particularly pain on distention of the bladder. These symptoms had progressed irregularly for 5 years. Excretory urography and routine urinalysis were normal. The Mazzini test for syphilis was negative. The bladder capacity was reduced and five typical Hunner's ulcers were seen by cystoscopic examination. A biopsy revealed chronic cystitis and culture of the urine found E. coli. A psychiatric consultant described the patient as having anxiety hysteria. Fulguration provided some relief and this was repeated 9 months later. Within 10 days of the second fulguration all symptoms returned and silver nitrate instillations were then used with variable temporary relief.

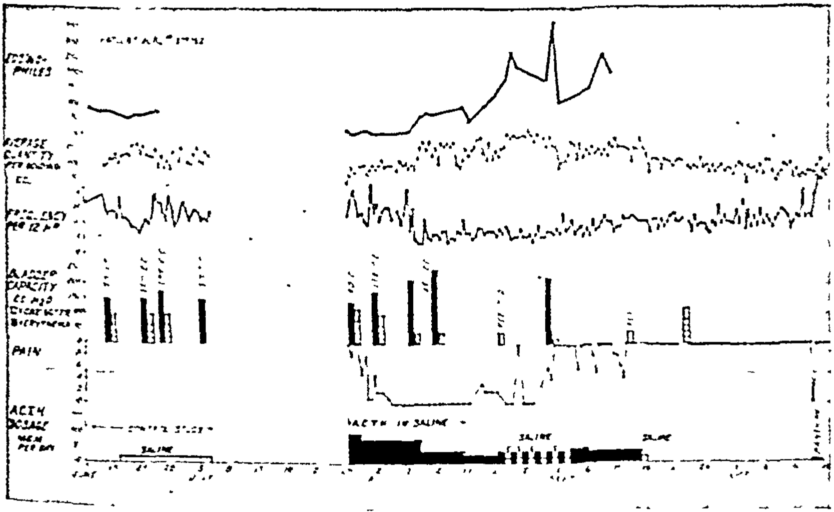

FIG. 5

The patient was not seen again for over 4 years during which time she had been treated in other hospitals with irrigations and fulguration. Studies now demonstrated a small vesical capacity, several ulcers, and A. aerogenes in the urine. Another biopsy was reported as chronic interstitial cystitis. Acid fast bacilli could not be found on smear or culture. Excretory urography and the Mazzini test were normal. Fulguration provided relief for only 2 weeks. Vitamin E in daily doses equivalent to 300 mg. of alpha tocopherol was given for 3 months without improvement. Silver nitrate and cajeput oil instillations were tried without significant alleviation and no major change in cystoscopic appearance.

Six and one half years after she first visited the clinic (and nearly 12 years since first symptoms) she was admitted to the hospital for a trial of ACTH therapy (fig. 5). Excretory urography, chest x-rays, electrocardiogram, routine urinalysis, and examinations for acid fast bacilli in the urine, were within normal limits. A routine urine culture found Ps. pyocyaneus. Cystoscopic examination found three Hunner's ulcers on the floor of the bladder. The measured vesical capacity was 150 cc. Intramuscular injections of one to two cubic centimeters of saline were given 4 times a day, the patient being informed that this was the "powerful drug" of which she had heard. Frequency, nocturia, and average volume of micturition did vary according to her mental attitude, but during this nineteen day period the measured capacity varied only 25 cc, the cystoscopic appearance was unchanged, and pain was not alleviated (table 1). She was discharged and readmitted a month later in an unchanged condition (fig. 5). ACTH was administered as in the other two cases. Pain disappeared after 9 days of

TABLE 1. *Patient H. A., No. 375252 (Control)*

CONTROL DATE	FREQUENCY	AVE. VOL. OF MICTURITION	RX	ATTITUDE
6/16	19	84 cc	0	Complains of pain in bladder after cystoscopy. Anxious to begin ACTH
6/17	13	98 cc	0	Feels better since she entered hospital. Pain is less
6/18	14	116 cc	0	Very inquisitive about when ACTH will be given. Pain continues to subside
6/19	12	100 cc	Saline 1 cc q4H	Patient told she was receiving ACTH
6/20	12	130 cc	Saline only	Pain is less she thinks. She wonders when she will feel effects of ACTH
6/21	9	127	Saline only	She thinks "ACTH" is causing pain in legs, but feels much better
6/22	7	169	Saline only	Comfortable and without complaints
6/23	12	133	Saline only	Frequently remarks about effects of "ACTH" She fears she will be deformed. Complaining of pain in bladder
6/24	12	130	Saline only	
6/25	17	122	Saline only	Very discouraged about her condition. Feels "ACTH" is of no benefit
6/26	14	89	Saline only	Very discouraged and anxious
6/27	19	85	Saline only	She feels neglected and she thinks doctors aren't interested in her. She was reassured
6/28	9	85	Saline 2 cc q4H	Patient told she is getting double doses of "ACTH"
6/29		110	Saline only	Depressed but expresses hope that double doses of "ACTH" will help her
6/30	11	155	Saline only	Feels better and has less pain
7/1	15	108	Saline only	Feels much better and states that the double doses are doing the trick
7/2	11	135	Saline only	Much happier—states that she is feeling better than ever
7/3	11	110	Saline only	Cystoscopy caused recurrence of pain; patient expressed fear of return of severe pain
7/4	10	145	Saline only	Worried about caring for pain at home, and expressed anxiety about future

treatment, the ulcer could not be seen after 10 days, and the measured capacity had increased from 140 cc to 260 cc by the fifteenth day of treatment. The frequency and nocturia also decreased and generally the patient seemed to feel well. The dosage was gradually reduced but below a daily total of 40 mg. given in 4 divided doses the pain and ulcer returned.

TABLE 2

Time in days required to achieve maximal improvement

	PILOT STUDY			SECOND STUDY		
	Pain	Ulcer	capacity	Pain	Ulcer	capacity
Case 1	10	12	12	7	4	28
Case 2	5	12	12	5	18	18
Case 3	9	10	15			

Average. pain—7 2 days; ulcer—11 2 days, bladder capacity—17 days

Time in days for full recurrence

	PILOT STUDY			SECOND STUDY
	Pain	Ulcer	capacity	Pain, ulcer, capacity
Case 1	40	12	40	Symptoms recurred while on maintenance program
Case 2	26	5	40	Symptoms if ACTH less than 120 mgm. daily
Case 3	Rec. on RX	7	7	

Maximal measured bladder capacity achieved

PATIENT	VOLUME PRIOR TO RX	MAX CAPACITY ACHIEVED	INCREASE	DAYS
		Pilot study		
1	50 cc	150 cc	3×	12
2	45 cc	220 cc	4 84×	12
3	150 cc	250 cc	1 66×	15
		Second study		
1	110 cc	230 cc	2 09×	28
2	100 cc	185 cc	1 65×	18

The experiences in this case seem to confirm the impression that the improvements noted in cases 1 and 2 were not mere co-incidences. In addition, the benefit did not arise from hospitalization, rest, reassurance, and simple suggestion in either case 2 or 3. In fact, the psychologic situations were arranged so that one should not expect improvement unless the ACTH was the principal factor: for example, the last patient was discharged in a discouraged state and only by much persuasion did she return for another trial of what she thought was the same drug. Among the arrangements, the patients in case 1 and 2 were kept together in the same room. They constantly compared their responses. Patient 1 became euphoric and relieved on ACTH, while patient 2 only showed irregular marked fluctuations in the degree of pain (and some minor changes in frequency) on saline injections. Both understood they were receiving ACTH. During this period only patient 1 had objective evidence of improvement. In spite of such discouragement, patient 2 did subsequently improve both subjectively and objectively when the hormone was actually given but without her knowledge of any change in the character of the injections. However, the nonspecific effect of the euphoria produced by ACTH is a factor in these improvements. The magnitude of this factor relative to the possibility of more specific effects is not known (table 2).

It was particularly disappointing that a satisfactory maintainence program was not evolved. Full dosage of ACTH for months, even years, would not only be impractical and expensive, but dangerous. The impression was unavoidable that control was an all or none matter; except that it was most interesting to note that while the capacity dropped from its peak value, it did not return to its pretherapy low even when all of the hormone had been discontinued. Perhaps with a longer follow-up the capacity will be found to return to its pretreatment value, but at least the evidence from the 3 cases is that the capacity drops slowly after cessation of treatment. One might speculate that a combination of hormonal therapy with standard modalities might be found which would be satisfactory. Our experience with cortisone and progesterone is too limited for a reliable comment. Fortunately, Dr. John Dees[5] and his associates became interested in these clinical experiments and they are making a similar study with cortisone. Our results with ACTH are nearly the same as those obtained by Weaver and Tyler,[4] indicating a constancy of effect.

Undesirable reactions were observed in all 3 patients. Transient arthralgia, glycosuria, and euphoria, occurred in three; edema and agitation in two; and acne in one. A low salt (3 gm. daily) diet and 2 gm. of potassium chloride daily were administered when edema occurred and continued until the admission weight was regained.

This study does demonstrate that the parenteral administration of adequate doses of adrenocorticotrophic hormone improved the bladders of 3 patients with advanced and refractory chronic interstitial cystitis. This was accomplished without local treatment to the bladder and apparently regardless of the presence or absence of rest, reassurance, and simple suggestion. The response could be readily elicited a second time, in the two cases in which it was attempted but maintenance on a practical schedule was not attained.

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[4] Weaver, R. G. and Tyler, F. H.: The use of ACTH in interstitial cystitis (Hunner's ulcer), Proc. Second Clinical ACTH Conference, pp. 507–515. Philadelphia: The Blakiston Co., 1951

[5] Dees, John E.: Personal communication.

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CARCINOMA OF THE PROSTATE: RESULTS OF TOTAL PROSTATECTOMY

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Castration and the estrogens have had a profound effect upon cancer of the prostate but there is little evidence that these measures are curative. Surgery always has been considered the only method by which this disease could be cured. But total prostatectomy usually is recommended only when the tumor is at an early stage of development and preferably confined within the prostatic capsule. There is no way I know of by which a fair comparison can be made between these two methods of treatment, anti-androgenic therapy and radical surgery. For the former has been applied to cancer in many phases of its growth and the latter to carefully selected instances of tumors that seem to be localized to small areas within the gland or to neoplasms that for the most part give no evidence of a spread beyond the capsule of the gland. I know of no reported series of similar tumors that have been treated only by hormonal measures. The reported end-results of surgery find the patients clinically free of disease at different periods of time. Those reported alive after endocrine therapy leave the condition of the patient to one's imagination.

We know that some patients who have early cancer of the prostate survive for many years as a result of castration and the estrogens or with no treatment at all. The average duration of life of patients who have such early lesions, however, is not known.

If total prostatectomy is to be the accepted treatment for early cancer, the operation should meet certain requirements. The long-term postoperative survival rate without evidence of disease should be high enough to justify operation. Operative mortality and complications should be at a reasonable level. Urinary control should be of such a nature that these patients can lead an active life and not be denied to society.

One hundred total prostatectomies performed at the Massachusetts General Hospital during the past 20 years for suspected cancer have been reviewed (fig. 1). These are cases operated upon on our ward service and private patients of our own. About an equal or greater number of patients on other private services are not included. Although we have long been convinced that total prostatectomy is the best treatment for early prostatic cancer and have been alert for suitable cases, our series is not very large. It is noteworthy, however, that late years have shown a substantial increase in the number of these operations. Four times as many total prostatectomies were performed by us during the last decade as were done in the previous ten years.

Not all of these 100 cases were cancer. In spite of clinical evidence that cancer was present, no malignant disease existed in twenty-one. There were 79 proved

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cases of carcinoma. These 79 cases have been reviewed according to age, symptoms, pathological findings and end-results. The entire series of 100 cases has been studied concerning accuracy of diagnosis, operative mortality, postoperative complications and urinary control.

Age of patients. The incidence of early prostatic cancer at different age periods is of some interest. This disease in our series occurred less frequently during the periods of early middle age and old age. Its incidence before 60 years of age was 10 per cent and after seventy-five it was 16 per cent. Cancer of the prostate reached its peak between the ages of sixty and seventy-five. About three quarters of our cases occurred during that 15 year period. There was little difference in its incidence in the 5-year periods between sixty and seventy-five. The decline in incidence of the disease after seventy-five is, of course, modified by our reluctance to operate upon men beyond this age. The youngest patient operated upon was forty-two and the oldest was eighty-five. Four patients in our series were less than 55 years of age and three were eighty to eighty-five. These elderly men were operated upon before the days of endocrine therapy.

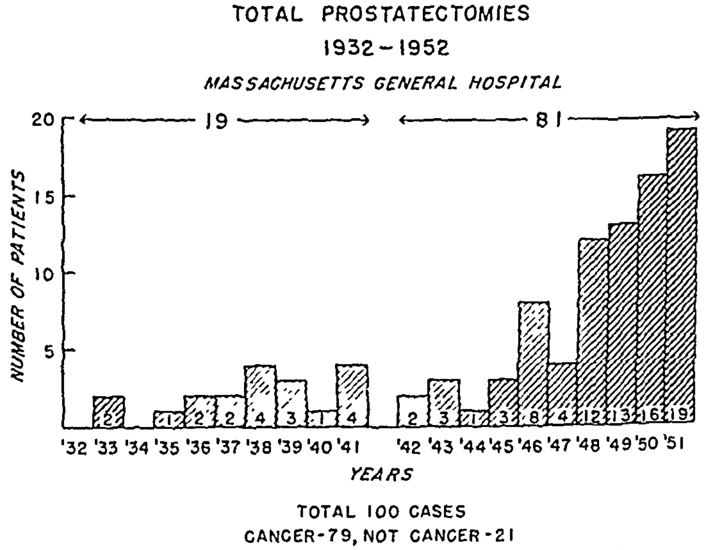

FIG. 1. Yearly record of 100 total prostatectomies for suspected cancer, 1932–1951 Massachusetts General Hospital.

Symptoms. It would be well if there were more general recognition of the fact that *early cancer of the prostate produces no symptoms.* Such symptoms as are present when this disease is at an early stage usually are due to an associated benign hypertrophy. Benign enlargement of the gland was present in over one-half of the patients in this series with symptoms of obstruction, frequency and hematuria. Bleeding was an infrequent symptom and was due to causes other than the cancer. Forty-four per cent of our patients had no symptoms, their lesion being discovered on routine physical examination. Certainly this is an argument for periodic rectal examination in men over 50 years of age.

Diagnosis. Every urologist is faced with the problem of making an accurate diagnosis of early prostatic cancer. We should pride ourselves on our ability to do this better than others. But how accurate are we and what are the best methods of arriving at a correct diagnosis?

Present methods of making a diagnosis of this disease are: 1) rectal palpation, 2) cytological examination of expressed prostatic secretion, 3) needle biopsy, 4) perineal exposure and frozen section. A discussion of our own proficiency in diagnosis is presented.

Rectal palpation. The accuracy of this simple diagnostic method in our hands is as follows: Of 100 total prostatectomies, rectal examination suggested malignancy in ninety-four. Six patients were operated upon by subtotal prostatectomy under the impression that their lesions were benign. Histological examination proved these glands to be malignant and total prostatectomy was later carried out. Twenty-one patients had benign lesions. Rectal examination, then, was correct as a diagnostic measure in 73 per cent of our cases and misleading in 27 per cent.

Cytological examination. We have had little experience with this method of diagnosis. In advanced cancer many positive diagnoses doubtless can be made. In early cancer, however, it seems doubtful if this method can be very accurate. No reports on the cytological diagnosis of *early* prostatic malignancy are available. Since these neoplasms may arise in small areas of the posterior lobe or in a lateral lobe near the capsule, it seems doubtful that cytological examination should be accurate in many such cases. If this method of diagnosis is to be limited only to advanced instances of malignant disease, it will be of little use in the present consideration. Our own accuracy in all cases of prostatic cancer by cytological examination has been about forty per cent. We are seeking more information concerning the cytological diagnosis of early cancer of the prostate.

Needle biopsy. This method of diagnosing early cancer has been cried down by many clinics. Its accuracy, in our hands, had depended largely upon the enthusiasm of the examiner, his close cooperation with the department of pathology, and the care with which the tissue is produced.

The most that can be said for needle biopsy is that when it is positive, the patient does have cancer. Negative or unsatisfactory reports are of no value in excluding cancer.

In this discussion, needle biopsy is limited to cases that had total prostatectomies. Some patients had negative needle biopsies who did not have total prostatectomies. Since none of these patients were later found to have cancer, as far as I know, the accuracy of the procedure probably is better than our figures indicate.

Needle biopsy was performed in twenty-six of our cases. It was positive and was proved cancer in 16 patients. It was never positive when the patient did not have cancer. It was reported negative and was proved cancer in 4 cases. It was reported negative and was proved not cancer in 3 cases. Needle biopsy, then, was correct 73 per cent of the time (19 of 26 cases) and wrong or unsatisfactory 27 per cent of the time (7 of 26 cases). Since needle biopsy was no more accurate than rectal examination in our hands one may fairly inquire why go to the trouble of this not too accurate procedure? The answer is that there is great comfort in a definite histological diagnosis of cancer before total prostatectomy is performed.

Perineal biopsy and frozen section. This has been the most dependable and most accurate procedure. Its advantage consists in the removal of adequate tissue by direct approach to the prostate. But it does necessitate operation. In cases where the frozen section was reported negative and we were satisfied that no cancer was present I have seen no harm result from the operation.

Perineal biopsy was performed in thirty-six of the 79 cases of prostatic cancer. A report of cancer was received in thirty-two. Total removal of the gland and histological examination proved that cancer was present in thirty-one of these cases. In one case where frozen section was reported positive, examination of the entire gland failed to demonstrate malignancy. In 2 cases, the frozen section failed to show cancer and the totally removed prostate also gave no evidence of malignancy. In 2 cases where the frozen section was reported negative, the totally removed gland was proved malignant.

TABLE 1. *Diagnosis*

	RIGHT	WRONG
	per cent	*per cent*
Rectal examination	73	27
Needle biopsy	73	27
Perineal biopsy. .	91.6	8.4

Perineal biopsy, therefore, was correct in thirty-three of 36 cases or 91.6 per cent. It was wrong in 3 cases or 8.4 per cent. This method, then, had a considerable degree of accuracy. Its errors may have been due to the submission of insufficient tissue to the pathologist or to the difficulties of making an accurate diagnosis from sections that are less well fixed and stained than paraffin sections.

In forty-six of our 100 total prostatectomies, no biopsy of any kind was obtained. In these cases, the operator depended upon his preoperative impression from rectal examination that the gland was malignant and more especially upon the consistency of the prostate at the time of perineal exposure. That such impressions can be quite inaccurate is evident from the fact that without the benefit of any histological examination, the operator was correct 58.7 per cent of the time (27 of 46 cases) and incorrect 41.3 per cent of the time (19 of 46 cases). See table 1. When the operator depended upon his own judgment alone, he was wrong almost as often as he was right and proceeded with an unnecessarily radical operation.

In view of these facts, it seems unwise to embark upon radical surgery of the suspected prostate without definite histological evidence of cancer. The best way of being certain about this is by perineal exposure and frozen section.

Operation. As a rule, we are reluctant to advise total prostatectomy in men over 75 years of age. Most of the patients in this series who were beyond seventy-five were operated upon before the work of Charles Huggins. The operative technique used by us has been essentially that originally devised by Dr. Hugh Young.

Total prostatectomy by the retropubic route has had less appeal to us. A combined abdominoperineal operation, on the other hand, we have used 16 times. This we have done partly from curiosity to see how it would work, but it was usually done in cases where the cancer was associated with a considerable degree of benign hypertrophy. This, I believe, is a valid reason for the combined procedure.

Pelvic lymph node dissections were performed on 6 patients. Positive nodes were present in two or 33.3 per cent. It is interesting how closely this figure corresponds with the 34.5 per cent death rate by cancer within a 5-year period after operation as shown later.

A few points about the operation itself may be stressed. The gland should be freed from its attachments with as little manipulation as possible. This is easier said than done. The rough handling the prostate receives is a drawback to the operation. Tissue removal should be as radical as possible and should include Denonvilliers' fascia, *all* of the seminal vesicles with intervening tissue. The ureteral orifices must be clearly visualized and avoided. A good anastomosis between bladder neck and membranous urethra makes for a short convalescence and lessens the chance of stricture.

The perineal position is a strain on elderly men with impaired circulatory systems and we have been obliged to stop the operation at times because of this. Great care must be used to avoid pressure upon the shoulders to minimize the very unpleasant complication of brachial palsy.

Postoperative mortality and complications. These were at a reasonable level in these 100 total prostatectomies. There were 5 deaths, a mortality of 5 per cent. Two deaths were from postoperative shock and hemorrhage. Two deaths resulted from ligation of a ureter, with an associated rectal tear in one. One death was attributed to cardiac failure.

Complications were not too common. The rectum was damaged in 3 cases. Two were successfully repaired but one is included in the postoperative deaths. Rectal injury is a serious complication not to be taken lightly. Three patients had postoperative strictures at the anastomosis between the bladder and the membranous urethra. All responded to dilatation. Two perineal fistulas healed with time. Two patients had epididymitis. One postoperative hemorrhage necessitated cystotomy. A ureter was damaged in 3 patients, two died, the third had the ureter successfully re-implanted into the bladder. Brachial palsy followed operation in 2 patients, a distressing and unnecessary event. One patient with postoperative pneumonia recovered.

The incidence of venous phenomena following operation in this older age group is important and interesting. We have been especially alert to thrombo-embolic phenomena and have campaigned vigorously to prevent deaths from pulmonary embolism. There have been no deaths from pulmonary emboli in this series of 100 total prostatectomies. Perhaps some deaths have been averted by our vigilance. In 4 cases thrombophlebitis developed and in these patients the femoral veins were promptly ligated. None died of a pulmonary infarct. Prophylactic femoral vein ligations were done 6 times on patients who had large varicosities of the legs or who had exceptionally poor circulatory systems. In 1939 to 1940, we took no precautions to prevent embolism, and fatal pulmonary emboli occurred in 2.64 per cent of all of our operations on the prostate. Of a total of 22 deaths in these 2 years, eight or about 36 per cent were due to fatal emboli. On this basis we may have averted two or three deaths since 1940.

Urinary control. The popularity of total prostatectomy will depend greatly upon whether patients are continent or incontinent. A price any patient may have to pay after this operation is imperfect urinary control. This is of major importance to the patient and may be a factor in his medical adviser's consent to the operation. Adequate urinary control, then, is important.

What is adequate control? The interpretation of this seems to vary with the physician who writes the follow-up notes upon the patient's record. The doctor who performed the operation and then sees the patient in the follow-up clinic is prone to rate control good if the patient can start and stop the urinary stream at stern command. If, however, this patient wets himself at the slightest effort, urinary control certainly is not good. The true state of affairs is best determined from the notes of several observers.

Between complete continence and complete incontinence there are shades of urinary control. These are not easily classified. Three headings, however, may suffice: 1) incontinent, meaning that the patient wears a bag or clamp; 2) fair, if he wears a pad or a diaper; 3) good, means normal or nearly normal control with at the most some degree of stress incontinence or minor leakage. Those classified as fair or good must be dry at night.

In the immediate postoperative period, urinary control often is poor. Twenty-three per cent of our patients were incontinent when they were discharged from the hospital. Seventy-two per cent had fair or good control. This is a high price to pay. Fortunately, however, with time, many patients regained better control. About one-half of those who were incontinent eventually dispensed with bag or clamp. Twelve patients remained incontinent. Seventy-two patients eventually had good control. In nine it was fair. The remaining 7 patients died before their continence could be fairly evaluated. Of 93 patients who survived long enough to tell about their continence, eighty-one or 87 per cent had good or fair control. Twelve or 13 per cent were incontinent. Thirty-five patients had normal urinary control.

Pathological examination. We have felt that useful facts could be learned by a careful pathological study of the tissues removed by total prostatectomy. In this we have the close co-operation of our department of pathology. Sections of all lobes of the gland are taken. Tissue from the bladder neck and seminal vesicles are studied and sections are examined for perineural and capsular invasion. Large sections of the entire gland are stained and mounted. A correlation of these facts with years of follow-up should be of value. Only in the past 3 years have we had the advantage of such thorough examination.

Areas involved. In the 79 cases of cancer it was demonstrated that in 20 cases only one lobe of the prostate contained cancer. More than one lobe was involved in 25 cases (fig. 2). There was no record of this fact in thirty-four. In spite of the selection of early cases of prostatic cancer, therefore, the tumor had already invaded adjacent areas, or arose independently in more than one lobe in over one-half (55.5 per cent) of our cases where this information was available. Although clinical examination had suggested that only one small area of the gland contained cancer, not infrequently pathological examination showed tumor in other areas. This probably is not an uncommon feature.

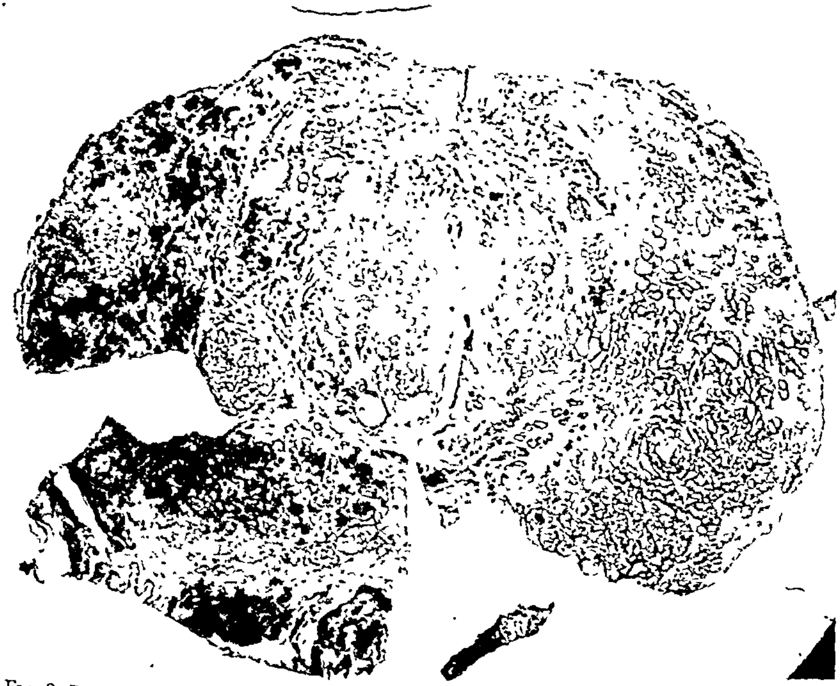

FIG. 2. Section of entire prostate. Photomicrograph low power. Dark stained areas are carcinoma. Areas of cancer are present in posterior lobe and right lateral lobe. Note small area of malignancy also in left lateral lobe just beneath capsule. Clinically, patient had small indurated area in right lateral lobe. Biopsy taken from right lateral lobe.

Perineural invasion. In the 79 cases of total prostatectomy for cancer, perineural invasion was reported present in 20 cases, absent in eight and not reported in fifty-one. Although many sections were not examined for this feature, the fact that it was present in 25.3 per cent of the cases and absent in 10 per cent suggests that perineural invasion is fairly frequent. When this feature was specifically looked for, it was present in 71 per cent. In our 41 cases of prostatic cancer operated upon more than 3 years ago, perineural invasion was reported present in eight, absent in eight and not reported in 25 cases. From these meager statistics I have attempted to draw some conclusions.

When perineural invasion was present in patients operated upon three or more years ago, one patient, or 12.5 per cent, died of cancer within 2 years. Since this patient had involvement of the bladder neck and seminal vesicles and was a very questionable candidate for operation, the presence of perineural invasion seems unimportant. Other patients whose tumors showed perineural invasion were all alive from 4 to 9 years after operation and clinically free of disease with one exception. This man has lived 9 years since operation but has now a hard nodule in the pelvis that suggests recurrence although recent needle biopsy produced no tumor cells.

No evidence of perineural invasion was reported in 8 cases. Two or 25 per cent died of cancer within 3 years of operation but in both the seminal vesicles were invaded by tumor. Four patients are alive from 5 to 8 years after operation and two have died of causes unrelated to their prostatic lesion.

There is little evidence from these inadequate figures that perineural invasion has prognostic significance. I suspect that its presence within the prostate does not necesssarily mean a spread of tumor cells beyond the gland itself. Tumor invasion of the lymphatics along the seminal vesicles probably is considerably more significant.

Capsular invasion. We sought to determine the importance of a spread of cancer to the prostatic capsule. In all 79 cases of total prostatectomy for cancer, capsular invasion was reported present in twenty or 25.3 per cent, absent in eight or 10.0 per cent, and not reported in fifty-one or 64.7 per cent. Although many of our early cases were not examined for this feature, capsular invasion seems to occur fairly frequently. When capsular invasion was specifically looked for, it was present in 71 per cent of the cases.

Of the 41 cases operated upon, more than 3 years ago, capsular invasion was present in 10 or 24.4 per cent. None of these 10 patients died of prostatic cancer. Eight have lived from 4 to 8 years clinically free of recurrent disease. One died of cancer of the sigmoid. One is alive 9 years since operation with possible, though unproven recurrence.

These figures suggest that capsular invasion is present fairly frequently but is not of great prognostic importance.

Involvement of the seminal vesicles. While perineural and capsular invasion by these neoplasms seemed to have little prognostic significance, it was thought that tumor invasion of the seminal vesicles probably was serious. Our studies seem to bear this out.

The seminal vesicles were completely removed in sixty-three of our 79 total prostatectomies for cancer. The vesicles were not removed or were only partially removed in sixteen. Partial removal was considered the equivalent of no removal at all. Tumor invasion was present in 20 patients whose vesicles were removed. In 36 patients no invasion was found. No report was received about the vesicles in seven. In twenty or 35.7 per cent of 56 cases whose vesicles were removed and concerning whom we had reports from the pathology department, invasion of the seminal vesicles was present.

There is a strong tendency, therefore, for these tumors to invade the seminal vesicles.

The seriousness of tumor invasion of the vesicles is illustrated by the 41 patients who were operated upon three or more years ago. In thirty of these the seminal vesicles were completely removed and they were not removed in eleven.

In seven of the 30 patients, the vesicles were invaded, no invasion was reported in nineteen and no report was given in four. In seven or 26.8 per cent of those concerning whom we had this information, the seminal vesicles were invaded by tumor. When such invasion was present, two or 28.5 per cent died of cancer within 2 years. In the 19 cases where no invasion was found, two or about 10 per cent died of cancer, one in 4 years and one in 7 years. It seemed, therefore, that invasion of the seminal vesicles was of serious import.

The effect of removal of the vesicles was studied in the 41 patients operated upon three or more years ago. Of 30 patients whose vesicles were completely removed five or 16.6 per cent died of cancer in from 1 to 7 years. (Invasion was present in seven.) Of 11 patients whose vesicles were not removed, six or 54.5 per cent were dead of cancer in from 1 to 5 years.

TABLE 2. *End Results: Over 3 years postoperatively, 41 patients*

	CASES	PER CENT
Alive and apparently well for 3 years	26	63.4
Alive with disease	2	4 9
Dead or not followed (1)	13	31.7
Dead of cancer	7	17 0
(Later died of cancer, 3)		

TABLE 3. *End results: Over 5 years postoperative, 29 patients*

	CASES	PER CENT
Alive and apparently well	15	51 7
Alive with ? of disease	1	3.5
Dead	13	44 8
Dead of cancer	10	34.5
(Later died of cancer, 1)		

This high death rate from cancer among those patients whose vesicles were not removed argues strongly in favor of complete removal of the seminal vesicles regardless of their gross characteristics at or before operation.

End results. Cancers of the prostate are variable. The disease spreads quickly and is rapidly fatal with some individuals while in others its progress is so slow that its presence seems of little importance when life expectation is not long. Some of our patients who survived the 3 or 5-year period clinically free of cancer died of their disease in subsequent years. One patient, well for 4 years after operation, developed evidence of recurrence in his pelvis but with stilbestrol has remained active for over 9 years since operation.

Three year follow-up. Forty-one patients had total prostatectomies previous to 1949. Twenty-six or 63.4 per cent were alive and clinically free of disease at the end of 3 years (table 2). Two were alive with disease. Twelve were dead and one could not be followed and is presumed dead (31.7 per cent). Six we know died of cancer and the one unfollowed case is counted as having died of cancer (17.0 per cent).

Six patients had castration and estrogens. One was castrated at the time of total prostatectomy and is alive 9 years later with possible recurrence. Others had anti-androgenic measures added to total prostatectomy at some time after operation but survived less than 2 years.

Five year follow-up. Twenty-nine patients had total prostatectomies five or more years ago (table 3). Fifteen or 51.7 per cent were alive and clinically free of disease at the end of five years. Thirteen or 44.8 per cent were dead. One was living with possible recurrence. Ten or 34.5 per cent had died of cancer. Of the fifteen 5-year survivors only one has subsequently died of cancer and this was 6 years after operation. If a 5-year postoperative period has been safely passed, the chance of recurrence seems rather small.

CONCLUSIONS

There is an increasing tendency to favor total prostatectomy in the treatment of early cancer of the prostate. During the past 10 years we have performed four times as many of these operations as in the previous decade. A histological diagnosis of cancer should be obtained before total prostatectomy is performed. Perineal exposure and frozen section is the most reliable method of diagnosis. Perineural and capsular invasion seem to have little prognostic significance. Invasion of the seminal vesicles, however, seriously affects prognosis. The seminal vesicles always should be removed completely.

Postoperative mortality and complications have been reasonably low. Functional results after operation are sufficiently good, I believe, to justify the procedure.

Fifty-one and seven-tenths per cent of our patients after operation have survived for 5 years clinically free of cancer.

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ERYTHROPLASIA OF QUEYRAT

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Erythroplasia of Queyrat is a precancerous lesion involving the glans penis usually, but which may involve the coronal sulcus and the prepuce, of chronic nature and characterized by the appearance and persistence of slightly sensitive red plaques lightly infiltrating the mucous membranes. The lesion, although relatively rare, slowly and progressively changes from a precancerous to a malignant one.

Paget in 1874 described an analogous type lesion "Paget's Disease of the Nipple" and believed that a similar type dermatological disturbance might be observed on other parts of the body. Tarnowsky described a comparable lesion in 1891. Fournier and Darier in 1893 introduced the lesion into French literature, limiting the lesion to the penile site and naming it "Epithelioma Papillaire."

In 1911 Queyrat described the same lesion stating, "This is an affliction of chronic nature, characterized by the appearance and persistence of red plaques, non-painful and slightly sensitive, accompanied by light, superficial infiltration of the mucous membrane, and having a tendency in certain cases to degenerate toward an epithelioma type lesion . . . which because of the coloration, infiltration of the tissues and because of the similarity to leukoplakia, a comparison of which is found even in the evolution of the epithelioma, I propose to give this lesion the name of erythroplasia of the glans."

The disease was introduced to American literature by Sulzberger and Satenstein in 1933. In 1936 Irgang and Alexander reported the first case of a Negro in the literature.

Because of its location the lesion enters into the realm of the urologist, behooving the latter to not only be acquainted with the pathology in question but also to be proficient with the most adequate corrective measures.

The majority of authors consider the etiology as being essentially unknown, although irritation, trauma with or without scar formation, inflammation and syphilis have been postulated as predisposing factors.

Approximately 20 per cent or more of the cases reported, according to Montgomery, eventually develop into epitheliomas in situ. The condition is therefore classified as a precancerous lesion, a lesion not infrequently showing a remarkable paucity of histologic infiltration signs, namely, mitotic figures, marked inflammatory reaction, recurrent budding, dyskeratosis or other stigmata of incipient malignancy, yet eventually becoming malignant. In such a group are included erythroplasia of Queyrat, Bowen's disease, senile keratosis, arsenic keratosis, tar irritation and leukoplakia of various mucous membranes. However such esteemed writers as Sutten, Sulzberger and Satenstein reject such a term, pro-

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Read at meeting of Chicago Urological Society April 24, 1952.

pounding that it is of statistical value only, and that a lesion is either totally benign or malignant from its conception. Ormsby and Montgomery believe that until more is known about the etiology of cancer, and since in precancerous lesions all transitions from a benign to a malignant histopathognomonic picture can be seen in the same or adjacent lesions for a given case, the term "precancerosis" as defined has a definite classical and pathological meaning and is of prognostic and therapeutic value.

In a review of the literature, some 260 cases having been reported throughout the world, one finds a predominance of males over females in a ratio of two to one. This is a disease of the second half of life; the range in the 260 cases was between 24–77 years, with a comparable average age of 48. Circumcised and noncircumcised cases are both included in the reported series. With respect to the latter, irritation may well be an important factor, being due to smegma irritation plus infection, while in the circumcised cases clothing irritation may be paramount in its production.

Erythroplasia of Queyrat is characterized by an irregular but sharply demarcated, round or oval, red, grossly lobulated, flattened yet slightly raised lesion that has a smooth velvety sensation, shiny appearance and a somewhat more firm consistency than the surrounding normal skin. There is only a superficial infiltration tendency. The lesion is moist only if associated with secretogenic surfaces. At times superficial erosions are noted as are marginal leukoplakia. The majority of male lesions are noted on the dorsal aspect of the glans, glans preputial portion and, to a lesser extent, on the inner preputial surface. In the female the predominant lesion is along the labia minora, interlabial furrow or on the labia majora, especially along the posterior fourchette. Occasionally it is seen on the clitoris and cervix. A single lesion is present in most cases, although at times several lesions have been noted and may attain 2–5 cm. in diameter. Even in multiple lesions there is a coalescing tendency over a period of time. The plaque may remain stationary for a varying amount of time, then increase in size. Rarely a temporary regression is observed.

A review of 260 cases revealed the average duration of the lesion to be 37 months, the shortest interval being 6 weeks and the longest 12 years.

Symptomatology may be minimal or at most nonincapacitating and of minor degree consisting of some itching, burning sensations. In advanced cases bleeding and adhesions to the prepuce may occur.

Histologically the most common type consists of a dyskeratotic type lesion with rete peg hypertrophy (metaplastic variety). A second type, the hyperplastic, reveals a strong acanthotic reaction with elongated interpapillary buds having minor ramifying qualities. A variable degree of inflammatory reaction is present in the cutis, often perivascular in location. The remarkable paucity of keratohyalin formation produces the gross reddish appearance. Both varieties may be present together as mixed types.

Diagnosis. A presumptive diagnosis may be made on the appearance and location associated with slow progression tendencies and a history of chronicity.

However, only by a biopsy is a definite diagnosis made, presenting an essentially characteristic microscopic picture.

A Kahn test, blood sugar, urinalysis, white and red blood count, vaginal smear, urethral smear and in a case of suspected chancre, a dark field examination are valuable adjunctives. The lesion must be differentiated from seborrheic dermatitis, lichen planus, syphilis (primary or secondary), carcinoma of the skin, sarcoid, contact dermatitis, recurrent herpes, dermatitis medicamentosa, granuloma inguinale, diabetic dermatologic changes, lupus tuberculosa, lupus erythematosis and Paget's and Bowen's disease.

The form of treatment utilized depends on whether the lesion is considered benign, precancerous or frankly malignant. If benign, a conservative local therapy of neoarsphenamine or borax solution irrigations, protective dressings, bland ointments and a mechanical tube preventing local irritation are utilized. Some men have used electrocoagulation, carbon dioxide freezing or local excision with variable degrees of success.

Most authors consider the lesion precancerous or malignant, requiring more radical measures. Surgical intervention appears to be then the only adequate form of treatment. A benign appearing early lesion may be handled satisfactorily by performing a partial amputation of the distal one-third of the penile shaft 2 cm. proximal to the lesion edge, followed by periodic office examinations for recurrences. In well advanced cases the only rational type of therapy consists of amputation of the entire penile shaft with removal of the regional lymph nodes. Exploration of the inguinal area for involved lymph nodes is always recommended since prognosis varies diametrically opposite to there being metastasis present. Electrocoagulation locally either alone or with x-ray therapy to lymph nodes has met with little success to date in advanced lesions.

CASE REPORT

We herein report the two hundred-sixty-first case of erythroplasia of Queyrat. A 79 year old white man entered the Presbyterian Hospital of Chicago, September 14, 1949, on the Herbst-Merricks urologic service. His complaint was a "gradual tightening of the foreskin" for the past 3 years. During this time two paraphimotic episodes had occurred. Circumcision had been refused twice. Now the foreskin could not be retracted and was becoming increasingly tender. Several previous hospital admissions had occurred for non-related conditions.

Physical examination revealed a stocky, well developed man. Blood pressure was 128/62. The eyelids were slightly injected. The abdomen was slightly protuberant. Upon rectal examination the prostate was normal in size but somewhat firm. The prepuce was tightly constricted. It could not be retracted. The adherent edges were swollen and angry looking. The distal aspect of the glans was superficially ulcerated. A finding of 50 leukocytes in the urine per low powered field was the only significant laboratory observation.

Circumcision by the dorsal slit, lateral flap method was performed. Dense adhesions were encountered in freeing the prepuce, revealing an ulcerated glans.

A relatively uneventful postoperative course ensued without urinary complications. The glans was slow to heal. Two areas in particular remained slightly raised, well circumscribed and reddish in color. They were moderately tender. After 22 days of various medicaments, the patient was discharged.

During the next 6 months various ointments and chemicals failed to bring about complete healing of the glans. The patient was seen by Dr. James H. Mitchell who took the photographs (fig. 1). He also obtained a biopsy which revealed erythroplasia of Queyrat with suspicions of malignancy.

On February 23, 1950, the patient was re-admitted to the hospital. The glans penis was reddened and injected in irregular regions with a dry, denuded area on the right lateral aspect, circumcribed, somewhat irregular in contour, very slightly raised, red, velvety and glazed in appearance with no particular induration. No inguinal adenopathy was noted. Urinalysis was negative.

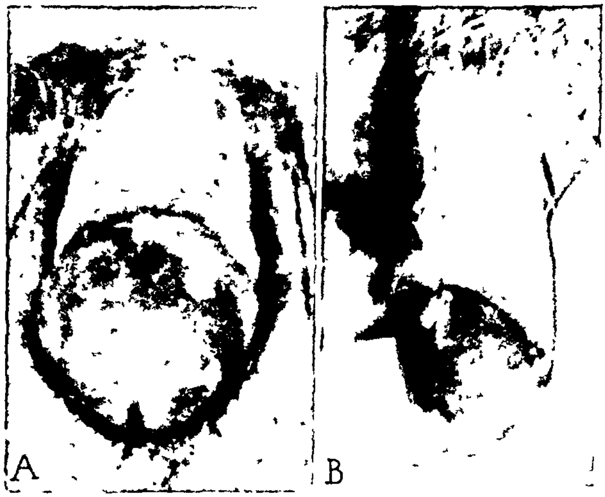

FIG. 1. Erythroplasia of Queyrat. *A*, dorsal view of gross lesion demonstrating irregular circumscribed, slightly raised red velvety glazed lesion. *B*, lateral view.

The penis was amputated the following morning. The incision was carried around 2 cm. proximal to the corona. The defect was covered by a frenular flap of skin with a cruciate stab wound through which the urethra was drawn. Some plastic induration was noted in the corpora. An inlying 5 cc Foley bag was placed in the urethra. Inguinal exploration revealed nothing of significance.

The postoperative course was uneventful. The catheter was removed on the eighth day. The new meatus has shown no tendency to contract.

The gross pathological description was that of a "glans penis with 1 cm. of tissue proximal, the glans being covered with multiple irregular leukoplakia appearing areas and on the dorsum a 4 mm. ulcerated area." A section taken through the ulcerated area revealed "areas where there is a complete atrophy of the epidermis and in some places even ulceration. At the margins of these atrophic areas there is squamous epithelium which has undergone moderate hyperplasia with the presence of dyskeratosis (fig. 2). One small epithelial pearl is seen directly beneath the stratified squamous epithelium in one area. The same inflammatory infiltrate as seen in the previous specimen occurs in a band-like manner directly beneath the epithelium and extends downward into the deeper tissues in the peri-vascular spaces. The infiltrate is composed primarily of lymphocytes but there are also a few polymorphs, eosinophils, plasma cells and macrophages in some areas. The present slides which number six reveal focal areas of erythroplasia. There is no evidence of spreading carcinoma in these slides. This specimen then represents portions of amputated penis on which a diagnosis of transitional cell carcinoma developing from an erythroplasia of Queyrat is made." (George M. Hass, pathologist.)

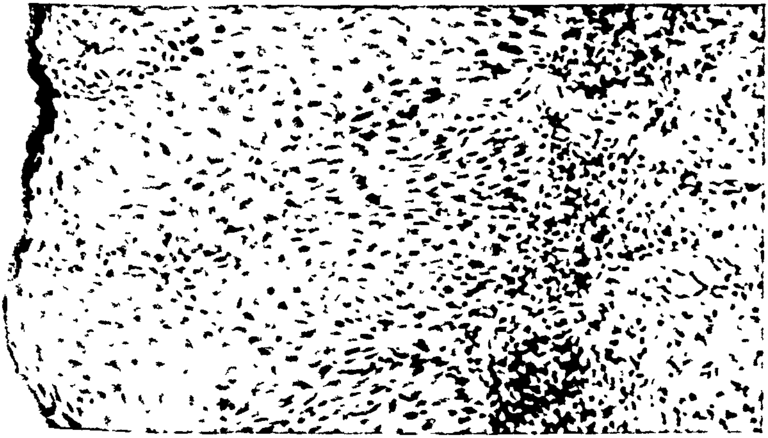

FIG. 2. Erythroplasia of Queyrat. Histological section revealing ulcerated areas, acanthosis of epidermis and, at margins, hyperplastic and dyskeratotic reaction of squamous epithelium. Cuff-like perivascular inflammatory infiltrate below epithelium is rather prominent.

The patient was discharged from the hospital some 19 days after operation with a nearly healed penile stump. There has been no recurrence of the condition to date.

CONCLUSIONS

Erythroplasia of Queyrat is a precancerous lesion involving the glans penis usually.

Twenty to forty per cent degenerate into malignant epitheliomas.

Etiology is essentially unknown, although irritation, inflammation and syphilis have been postulated as predisposing factors.

Males predominate in a 2 to 1 ratio.

Minor or absent symptomatology is the rule.

Biopsy of the lesion is essential.

The only adequate treatment available is amputation for an advanced case such as is reported here.

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QUEYRAT'S ERYTHROPLASIA WITH CARCINOMATOUS INVASION: REPORT OF AN UNUSUAL CASE

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Paget (1874), Tarnowsky (1891), and Fournier and Darier (1893) had successively discussed this disease. The presently known title was branded in 1911, when Queyrat presented his exhaustive study.

The etiology remains in the annals of obscurity. Lues has been suggested, and repeatedly denied, but chronic irritation has been advanced, although cases have been reported in circumcised people. Trichonomad and Treponema organisms have been suggested.

It is believed this case should be presented for two reasons: 1) The gross lesion in situ was undiagnosed because it did not even remotely resemble the classical description. 2) To prove that Queyrat's erythroplasia may not only be precancerous, but can be carcinoma in situ and, as in this case, can be invasive.

Until 1948, it was categorically acceptable that erythroplasia of Queyrat was not only precancerous, but that it was particularly prone to metastases, and must be recognized as such, because in spite of its benign appearance, it should be treated as cancer. In 1948, Sachs and Sachs presented 10 cases endowed entirely with strictly benign histopathological features, and therefore concluded the concept that erythroplasia is cancerous or precancerous is questionable.

The classical gross description is an habitually single, well defined area with brilliant red velvety surface, and little or no infiltration, occurring principally on the glans penis, vulva, mucous membranes of the mouth, and occasionally on the mucosal surface of the prepuce. Histologically, it is characterized by acanthosis, intracellular and intercellular edema of the epidermis, irregular and elongated rete pegs with many vacuolar cells and a fairly dense infiltration of round cells with vascular dilatation in the upper cutis.

REPORT OF CASE

M/Sgt. J. B. R., aged 39, appeared in the clinic on January 8, 1952 complaining of a small lesion on the left hand side, dorsal surface of the mucosal aspect of the prepuce, which had been present for ten years and had resisted all forms of local therapy. The lesion consisted of an oval shaped, slightly elevated, orange-brown area one and one half centimeters long with tiny, hard smooth papillary projections and multiple longitudinal fissures which burned and opened from time to time on intercourse and contamination by urine. Originally the lesion was characterized only by the fissures and induration, the oval shaped picture described, made its appearance approximately two months prior to the initial examination. There was nothing significant in the past history, and general physical examination, including special attention to the clinically available regional lymph drainage areas, was negative.

On January 10, 1952, under local anesthesia, the patient was circumcised well outside the pathological area, insuring eradication. The postoperative course was uneventful.

Figure 1, *A* reveals a low power section demonstrating the typical architecture of this entity, with all the neoplastic changes, compatible with intradermal carcinoma in situ.

Figure 1, *B* is a low power view of the area adjacent to *A* revealing invasion, vascular penetration was not demonstrable.

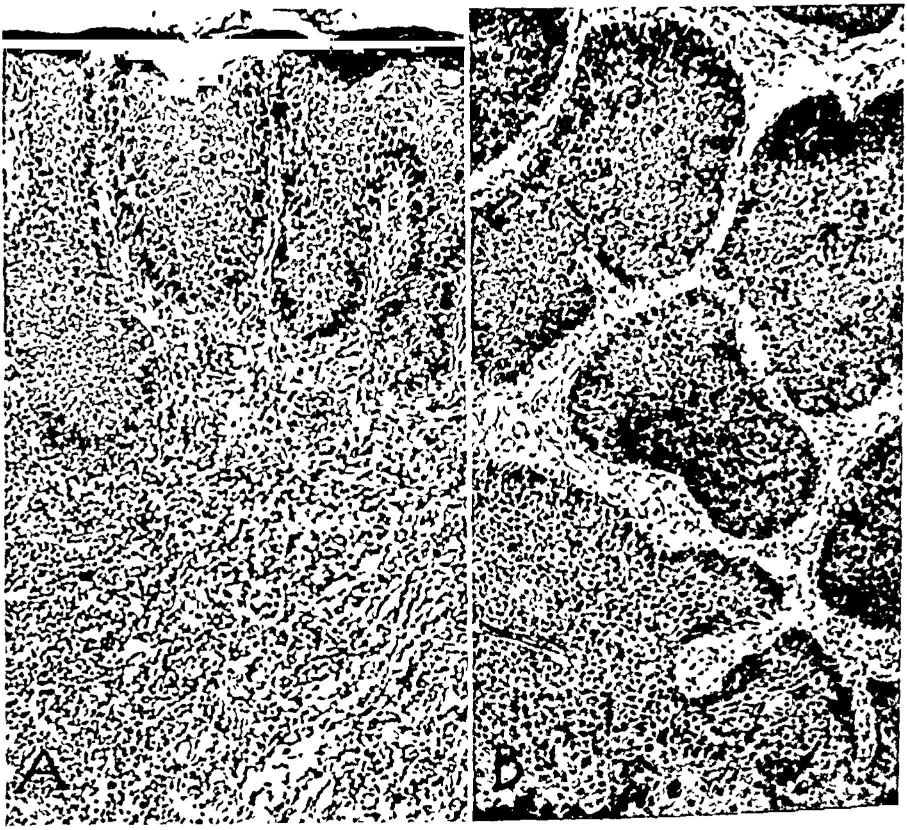

Fig. 1

In this case, eradication by circumcision was the treatment. Other methods are surgical excision and destruction with high frequency current. Sachs and Sachs, in their 10 cases, all devoid of neoplastic features, found local application of neoarsphenamine twice weekly for three weeks to be best, based on the hypothesis that the etiological agent was Trichonomad or Treponema with a relation to Vincent's infection.

This case has been presented to discourage any concept other than this: Queyrat's erythroplasia is a serious disease, and therapy must be governed accordingly.

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ACUTE SCROTAL APPENDICITIS

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Much has been written concerning acute appendicitis and the various normal and abnormal locations of the appendix. In view of the variability of the position of this structure, its finding as part of the contents of a hernia should not be particularly uncommon. As one scans the literature, however, he sees that reports of finding the appendix in the scrotum are very few. This paper is concerned with the unusual occurrence of acute vermiform appendicitis in the scrotum.

Keyes[1] reported the presence of the cecum and appendix in the scrotum in a large indirect inguinal hernia. Zambrana[2] reported a case of appendicular abscess localized in the scrotum. Recently Reif[3] reported an acute scrotal appendicitis in a 2½ weeks old boy. Although the condition must be fairly common, these are the few references to the acute appendix being found in the scrotum.

The appendix may be practically anywhere in the abdomen, in the fossa, pouches and canals thereabouts. Besides being found in the scrotum, in hernial sacs (inguinal) or in the thigh in a femoral sac, it has also been reported in the thorax.[4] If the hernia is a sliding one of the cecum, the appendix may be in the scrotum or thigh outside the sac. Babcock[5] has not infrequently found the appendix in a hernial sac, particularly that of a right inguinal hernia. He found a gangrenous appendix as the only occupant of a right inguinal hernia and has reported one appendix herniated into a left inguinal hernia. Left herniation of the appendix occurs as the result of complete or incomplete transposition of the viscera in most cases, there being in a few also dextrocardia.[6]

Ryan[7] in 1937 presented figures showing that of 8,692 cases of appendicitis, 11 or 0.13 per cent were found in the hernial sac. Coley[8] found that of 2,200 hernias operated, the appendix was found 17 times or 0.77 per cent. The finding of the appendix alone in a hernial sac is more unusual and Watson[9] found reports of only 53 cases in a series of 17,192 cases of hernia collected from the literature.

The appendix in the sac of a hernia would seem more likely to be acutely inflamed than is the appendix within the abdomen. True strangulation of the herniated appendix probably is unusual but can occur. The likely situation which occurs is that due to its greater exposure to trauma in the sac, mild recurring inflammatory changes give rise to a more acute process with resulting changes characteristic of acute suppurative appendicitis.

Read at annual meeting, Mid-Atlantic Section, American Urological Association, Philadelphia, Pa. April 18, 1952.

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The symptoms of hernia of the appendix usually are so mild that they are given little attention prior to the development of acute appendicitis and the diagnosis is practically never made before operation. There may be a history of recurrent bouts of abdominal pain and nausea but because of absence of tenderness is not usually attributed to the appendix. In the scrotal type the greatest attention is focused on the painful, reddened, swollen scrotum which usually overshadows any complaints referable to the abdomen. Most of the time a preoperative diagnosis of strangulated hernia or acute torsion of the testicle is made.

The following case is illustrative of three separate hernias among which the appendix was involved.

"A 6 month old Negro boy was admitted to the Philadelphia Hospital for Contagious Diseases on February 14, 1951 with a diagnosis of mumps. There was noticed also, a nonreducible mass in the left side of the scrotum which had never been seen previously. There was associated tachypnea and irritability, but no vomiting and normal stools were reported. There was also a reducible umbilical hernia which had been present for the past 5 months.

Pertinent physical findings on admission were, an acutely ill colored male infant, quite irritable and crying constantly. Temperature was 104, pulse 105 and respiration 50. Meningismus was present. The adbomen revealed marked distention with prominent tortuous veins of the abdominal wall. A large nontender reducible umbilical hernia was present but no other abdominal masses were palpated. Percussion was tympannic and no peristalsis was heard. The genitalia presented a large, tender, erythematous swelling markedly distorting the left side of the scrotum and not transilluminated. No bowel sounds were heard over this area. The diagnosis on admission was strangulated left inguinal hernia, reducible umbilical hernia.

Initial laboratory studies: hemoglobin, 6 gm.; red blood cells, 3,420,000; white blood cells, 19,600; polymorphonuclears 69 per cent; lymphocytes, 30 per cent; monocytes, 1 per cent; CO_2 combining power, 31 volumes per cent.

On the day of admission, under ether anesthesia, an oblique left inguinal incision was made (by a general surgeon) and dissection carried down to the mass in the scrotum. This was found to be an edematous and necrotic hernial sac communicating with a hydrocele. The testicle was involved in this same inflammatory process. Before any further surgery was performed in this area, the abdomen was entered by way of the umbilical hernia and the inguinal hernia examined from an intra-abdominal position. After it was established that the two lesions were separate, the hernial sac, hydrocele and testicle were all removed inguinally *en masse* and the defect in the inguinal region closed. The bowel appeared normal but some free fluid was noted in the peritoneal cavity. The umbilical hernia likewise was repaired.

Postoperately the infant was maintained with streptomycin 100 mg. every 6 hours, intravenous terramycin 100 mg. every 12 hours, whole blood and intravenous fluids with constant gastric suction. On the second postoperative day, the temperature was 102.2F, pulse 130, respirations 24. Bowel sounds were audible. The infant was started on surgical liquids orally with supplementary parenteral fluids and antibiotics continued.

On the third postoperative day the infant spiked a fever to 103.2F and cried constantly throughout the day. Some coughing was noted but he was taking and retaining fluids well. The abdomen was slightly distended but soft with active peristalsis. The left inguinal incision remained normal. At this time it was noted that the right side of the scrotum was swollen with a separate, firm, tender, olive sized mass immediately above the right testicle. The patient showed continued progress and was still eating and retaining food.

When this patient was first seen by the urologic consultant on the sixth postoperative day, the condition was essentially as noted in the foregoing paragraph. It was believed that he may have had a torsion of the left testicle and perhaps the mass on the right side was also a similar torsion, but because of the abdominal distention, there must be some relationship with the abdominal cavity. Exploration of the right side of the scrotum was advised.

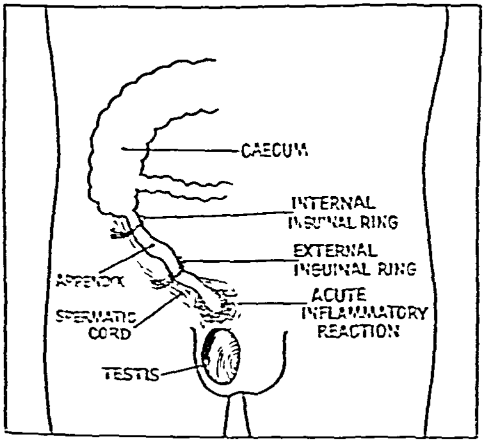

FIG. 1. Diagram showing location of acute appendix within scrotum

A second operation, one week following the initial one, was performed through a right inguinal incision extending down to the scrotum. A definite mass was found in the upper portion of the scrotum extending along the spermatic cord which was inflamed and edematous. The testicle did not appear to be directly involved. The testicle and cord were delivered and the inguinal canal opened. The mass was found adherent to the spermatic cord just above the testicle. The processus vaginalis was opened with difficulty due to considerable inflammatory reaction around the mass and cord close to the external inguinal ring. A tubular structure was noted (fig. 1) after further dissection, extending from the internal ring down to the inflammatory lesion. This tubular structure was further dissected free and found to be coiled on itself with a definite inflammatory and seminecrotic tip. The internal ring was enlarged, the cecum grasped and pulled down into view and the tubular structure was identified as the vermiform appendix. This was then easily removed by the usual technique, leaving the right spermatic cord and testicle intact. The hernia was then repaired and the wound closed.

Postoperatively, the infant received intravenous fluids and whole blood until the hemoglobin reached 11 gm. The patient never vomited; he urinated promptly and had normal stools throughout. Antibiotics were continued for 1 week postoperatively. Temperature ranged between 99–101F rectally for the first two days, then remained normal. The patient was discharged on the ninth postoperative day with both incisions well healed.

Pathological report (first operation): Microscopic examination of the tissue submitted revealed a recent hematoma at one edge of which there appeared to be organization characterized by fibroblasts and capillary proliferation into the edge of the blood clot. Further away from the edge of the blood clot the fibrous tissue had taken on a myxomatous pattern. Other sections revealed foci of necrosis in which there were numerous neutrophiles surrounded by similar myxomatous fibrous tissue, some of which showed evidence of recent proliferation with numerous capillaries and fibroblasts. In still other sections, poorly differentiated testicular tissue was noted in which the tubules were very small, the lining cells atrophic and no evidence of spermatogenesis was present. *Diagnosis:* 1) Gangrenous hernial sac; 2) infantile testis; 3) organizing hematoma.

Pathological report (second operation): Vermiform appendix, measuring approximately 11 cm. with a markedly inflammatory, edematous tip (2 cm.). Microscopic description was consistent with the diagnosis of acute suppurative appendicitis.

COMMENT

Certainly the general surgeon has the opportunity to see acute appendicitis within the scrotum fairly often in dealing with abdominal lesions and hernias. To the urologist on the other hand, it is quite uncommon. Because of the differential diagnostic problem involved, it is important that the urologist be aware of the condition. He is constantly dealing with acute inflammatory testicular lesions, torsion of the testicle, injuries of the scrotum and malignant disease of these organs. The knowledge that acute appendicitis within the scrotum can and does occur, may be an interesting fact for the urologist to hold in mind.

SUMMARY

A case of acute scrotal appendicitis is reported. The literature is reviewed and the various locations of the appendix are discussed. The problem of diagnosis and management are considered. Another case of scrotal vermiform appendicitis is added to the literature.

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SPERMATIC GRANULOMA OF EPIDIDYMIS: CASE REPORT

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In 1947, Steinberg and Straus,[1] referring to the published works of Oberndorfer[2] in 1931 and Orsos[3] in 1941, reported a case of chronic granulomatous epididymitis with sperm invasion of the interstitial tissues. They stated: "The incidence is probably much greater than these few reports would indicate." Friedman and Garske[4] added 9 cases involving the epididymis among their twelve spermatic granulomas reported in 1949.

The following case is, we believe, another example of this peculiar pathologic entity and is reported in some detail to confirm the observations of the previous authors and to focus the attention of the profession on the condition.

CASE REPORT

A. P., 214952, a 22 year old Negro, was admitted to the hospital on September 26, 1951 with a diagnosis of epididymitis, acute, non-venereal, cause unknown. In January 1951, the patient was struck in the left pubic area with no ill effects other than pain at the time. About four weeks later he noticed a small mass which was soft and non-tender in the left side of his scrotum. This gradually enlarged, and when in September 1951, it became a little tender the patient came to the hospital for treatment.

The patient had a moderate sized hydrocele of the left scrotum which was not under a great deal of tension. Several slightly tender nodules could be palpated in the head of the left epididymis. It was thought that there was a slight amount of fluid in the right tunica vaginalis also. The physical examination otherwise was not remarkable. The past history revealed no venereal disease. The patient was married in August 1949, but had had no children. Birth control by withdrawal had been practiced since marriage but the patient had always had satisfactory ejaculation. To his knowledge he had never had erotic epididymitis. He had three brothers and two sisters, one of which had children. The brothers were not married.

Blood and urine examinations were within normal limits. A chorionic gonadotropin test on the urine was negative. The serology was negative. Chest x-ray was essentially normal. As there was no history of venereal disease in this case, exploration was decided upon as it was believed that we were possibly dealing with a tumor of the epididymis.

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At operation the presence of a left hydrocele was confirmed. The epididymis was seen to be enlarged three times, injected, and edematous. There were several half centimeter clear cysts in the posterior tunica albuginea which previously had been thought to be nodules in the enlarged epididymis. Because of the possibility of tuberculosis and the poor appearance of the epididymis as to future function, an epididymectomy was performed and a hydrocele repair carried out. The postoperative course was uneventful.

Following this, two consecutive sperm counts showed a complete azospermia. Because of this total absence of sperm from the semen, the right side of the scrotum was explored and a similar, though less advanced, condition was found. Biopsies of both testes were taken at this time. In view of the azospermia it was felt that no harm could be done by taking a biopsy of the right epididymis. This was done and the wounds were closed. Again the postoperative course was uneventful and the patient was discharged from the hospital on October 29, 1951.

Pathologic examination of the left epididymis showed it to be 6 cm. long and up to 1 cm. in diameter after fixation in formalin. Toward one end of the structure there was nodular induration. The cut surface showed a sponge-like structure with milky fluid in the dilated tubular spaces. Microscopic sections through the indurated portion showed distention of the coils of the ductus epididymis and atrophy of the lining epithelium. The normal columnar epithelium was replaced by low cuboidal or in some places by flattened epithelium without stereocilia. Many of the coils were displaced or replaced by nodular granuloma (fig. 1, *A*) consisting of a central pool of spermatozoa lying free in the interstitial tissues and surrounded by epitheloid macrophages containing ingested spermatozoa or a granular yellow-brown pigment. In general, the interstitial tissues of the organ were widened due to fibrosis and a cellular infiltrate of lymphocytes, fibroblasts, and histiocytes. Other sections through portions of the organ not as severely involved showed an interstitial chronic inflammatory reaction and a few pools of extruded spermatozoa (fig. 1, *B* and *C*). In at least two places actual rupture of the distended wall of the tubule could be visualized with extrusion of masses of spermatozoa into the interstitial tissues of the epididymis. Large numbers of spermatozoa were present in the lumen of the ductus. The fibrous capsule of the organ was somewhat thickened. The presence of spermatozoa in lymphatics was not seen. In other sections of the organ there was no inflammatory reaction in the interstitial tissues; and where no rupture of the tubule was present the ductus epididymis was lined by tall columnar epithelium with normal stereocilia, except for a few coils distended by masses of closely packed spermatozoa which compressed the epithelium.

The biopsy of the left testis showed seminiferous tubules producing mature spermatozoa in a normal fashion. The interstitial cells of Leydig appeared normal. The biopsy of the right epididymis showed some dilatation of the ductus, the lumen of which contained spermatozoa. In places there was flattening of the lining epithelium, but not to the degree seen in the left epididymis. In a few places the interstitial tissues were widened and contained fibroblasts, lymphocytes, and macrophages with coarsely granular yellowish-brown cytoplasmic

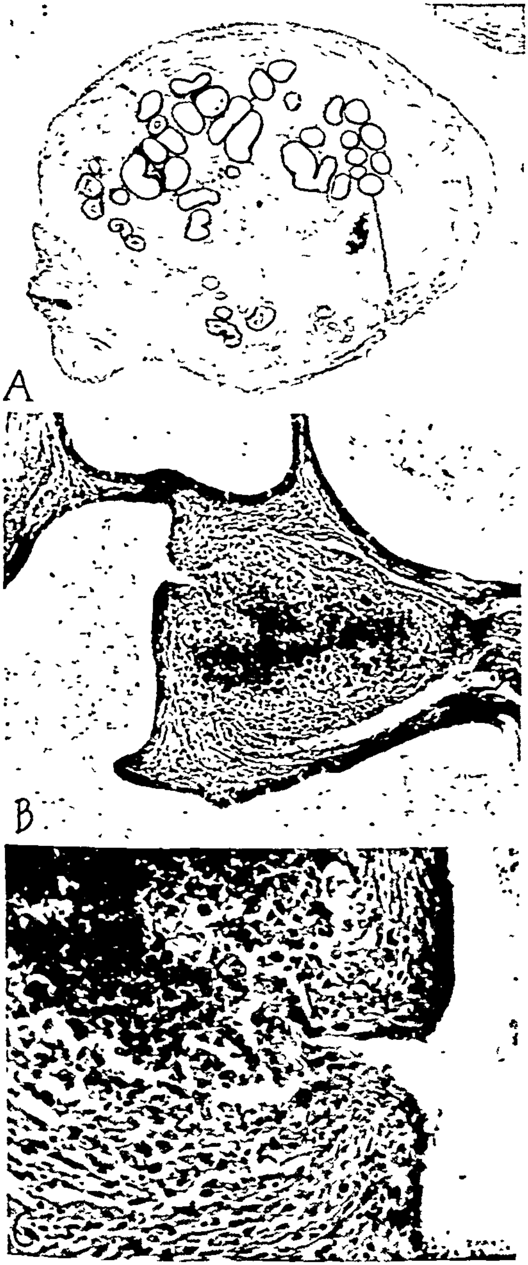

Fig. 1. A, cross section of left epididymis to show distention of duct, nodular granuloma placing coils of duct and interstitial fibrosis. Duct epithelium is atrophied. A. F. I. P. eg. No. 219705. 14113. × 10. B, left epididymis showing "blow-out" in atrophic wall of istended ductus epididymis. Irregular dark mass in interstitial tissue is puddle of extruded ermatozoa. A. F. I. P. Neg. No 219705. 14111 × 100 C, higher power view of B. Note trophy of epithelium of ductus. A. F. I. P. Neg. No. 219705. 14112.

particles. However, the nodular granulomas around puddles of undigested spermatozoa seen in the other epididymis were not present. Biopsy of the right testis showed decrease in the thickness of the spermatogenic epithelium. Most of the tubules were *not producing spermatozoa* and contained in their lumen desquamated epithelial cells. In some of the tubules, however, the production of mature spermatozoa could be observed. The interstitial cells appeared normal.

Pathologic diagnoses: 1) Spermatic granuloma of the left epididymis; 2) active spermatogenesis in the left testis; 3) interstitial fibrosis, probably healed spermatic granuloma, of the right epididymis; 4) diminished spermatogenesis in the right testis.

COMMENT

In previous reports there was frequently a history of operative active or accidental trauma or of epididymitis either gonorrheal or tuberculous. More than a third of the case histories, however, failed to reveal any factor that could reasonably be implicated in pathogenesis. Friedman's and Garske's tenth case was studied at autopsy and exhibited malformation and hypoplasia of the vasa deferentia and seminal vesicles. There was "compensatory" dilatation of the epididymis. In our case the dilatation of the ducts and atrophy of the epithelium, as well as the demonstration of "blow-outs" in the wall of the tubules suggest that possibly there may have been some partial obstruction to the excretion of sperm with rupture due to increased intraluminal pressure. There was a history of trauma to the left groin but no direct injury of the scrotum. The residuals noted in the right epididymis as well as the azospermia would indicate that the etiologic factor, whatever its nature, was acting bilaterally.

A better understanding of the pathogenesis will probably come with more complete study of further cases.

SUMMARY

The clinical and pathologic features of a case of spermatic granuloma of the epididymis are reported. The hope is expressed that further cases will be studied and reported with emphasis on pathogenesis.

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LEIOMYOSARCOMA OF THE SPERMATIC CORD

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Tumors of the testicle are relatively rare. They constitute about 0.6 per cent of all malignant tumors in men (Herman). Similarly, tumors of the epididymis are exceptionally rare and Thompson states that they are so rare that their existence might seem of more academic than clinical importance. Other intrascrotal tumors, those of the spermatic cord and the testicular tunics, occur somewhat more frequently.

When the pathological diagnosis was established in our case in January 1952, a search of the literature was carried out. According to Thompson's excellent review of the literature, the earliest known tumor of the spermatic cord was recorded by Cloquet in 1819. However, this report of a lipoma was meager and in 1845, Lesauvage contributed three authentic cases. In 1908, Patel and Chalier collected 110 cases of tumors of the spermatic cord in a review of the literature. In 1924, Hinman and Gibson were the first to classify such tumors. In 1939, Schulte, McDonald and Priestley presented a case of neurofibroma of the cord and reviewed the literature and reported 247 cases of tumors of the spermatic cord. There was a mathematical error and the total should have been 251. These included 2 cases of leiomyosarcoma of the spermatic cord. Then, from 1939 to January 1951, there were irregular reports of tumors of the cord.

Because of the rarity of leiomyosarcoma of the spermatic cord, it was decided to report our case discovered in January 1952. The two cases listed in 1939 by Schulte et al. consist of a case reported by Thompson seen in 1920 (this tumor appeared histologically to be a myoma but because of repeated recurrences was classed as a leiomyosarcoma). The other case of leiomyosarcoma of the spermatic cord could not be found. Leiomyoma of the spermatic cord is almost as rare and only 6 cases have been reported to date, seven if Thompson's case is regarded on histological findings only.

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particles. However, the nodular granulomas around puddles of undigested spermatozoa seen in the other epididymis were not present. Biopsy of the right testis showed decrease in the thickness of the spermatogenic epithelium. Most of the tubules were not producing spermatozoa and contained in their lumen desquamated epithelial cells. In some of the tubules, however, the production of mature spermatozoa could be observed. The interstitial cells appeared normal.

Pathologic diagnoses: 1) Spermatic granuloma of the left epididymis; 2) active spermatogenesis in the left testis; 3) interstitial fibrosis, probably healed spermatic granuloma, of the right epididymis; 4) diminished spermatogenesis in the right testis.

COMMENT

In previous reports there was frequently a history of operative active or accidental trauma or of epididymitis either gonorrheal or tuberculous. More than a third of the case histories, however, failed to reveal any factor that could reasonably be implicated in pathogenesis. Friedman's and Garske's tenth case was studied at autopsy and exhibited malformation and hypoplasia of the vasa deferentia and seminal vesicles. There was "compensatory" dilatation of the epididymis. In our case the dilatation of the ducts and atrophy of the epithelium, as well as the demonstration of "blow-outs" in the wall of the tubules suggest that possibly there may have been some partial obstruction to the excretion of sperm with rupture due to increased intraluminal pressure. There was a history of trauma to the left groin but no direct injury of the scrotum. The residuals noted in the right epididymis as well as the azospermia would indicate that the etiologic factor, whatever its nature, was acting bilaterally.

A better understanding of the pathogenesis will probably come with more complete study of further cases.

SUMMARY

The clinical and pathologic features of a case of spermatic granuloma of the epididymis are reported. The hope is expressed that further cases will be studied and reported with emphasis on pathogenesis.

Acknowledgement: Photomicrographs were prepared at the Armed Forces Institute of Pathology.

108 S. Washington, Bloomington, Ind.

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LEIOMYOSARCOMA OF THE SPERMATIC CORD

H. NIELS WESSEL

From the Urological Section of Surgical Service, Veterans Administration Hospital, Columbia, S. C.

Tumors of the testicle are relatively rare. They constitute about 0.6 per cent of all malignant tumors in men (Herman). Similarly, tumors of the epididymis are exceptionally rare and Thompson states that they are so rare that their existence might seem of more academic than clinical importance. Other intrascrotal tumors, those of the spermatic cord and the testicular tunics, occur somewhat more frequently.

When the pathological diagnosis was established in our case in January 1952, a search of the literature was carried out. According to Thompson's excellent review of the literature, the earliest known tumor of the spermatic cord was recorded by Cloquet in 1819. However, this report of a lipoma was meager and in 1845, Lesauvage contributed three authentic cases. In 1908, Patel and Chalier collected 110 cases of tumors of the spermatic cord in a review of the literature. In 1924, Hinman and Gibson were the first to classify such tumors. In 1939, Schulte, McDonald and Priestley presented a case of neurofibroma of the cord and reviewed the literature and reported 247 cases of tumors of the spermatic cord. There was a mathematical error and the total should have been 251. These included 2 cases of leiomyosarcoma of the spermatic cord. Then, from 1939 to January 1951, there were irregular reports of tumors of the cord.

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frequent than fibromas but they have a similar origin and present a similar clinical appearance. The following is a case report of a leiomyoma of the spermatic cord which has apparently undergone sarcomatous degeneration.

CASE REPORT

O. C., aged 36, a Negro, was admitted on January 10, 1952, to V. A. Hospital, Columbia, S. C., with a history of a progressively enlarging mass in the right scrotum. The patient stated that 9 years before admission he fell and injured his scrotum. He had pain in the right testicle for approximately 24 hours but noted no swelling. Four months later, the patient was hospitalized for food poisoning and while hospitalized, patient again had pain in the right testicle, this time with radiation of the pain into the lower abdomen. At that time patient claimed he felt a small "lump" on "top of" the right testicle. The pain subsided in several days but the "lump" persisted and in the next 8½ years the lump on top of the right testicle slowly and steadily increased in size. The pain did not recur but on January 7, 1952, the patient consulted his local medical doctor because of dragging sensation in the right scrotum due to the mass.

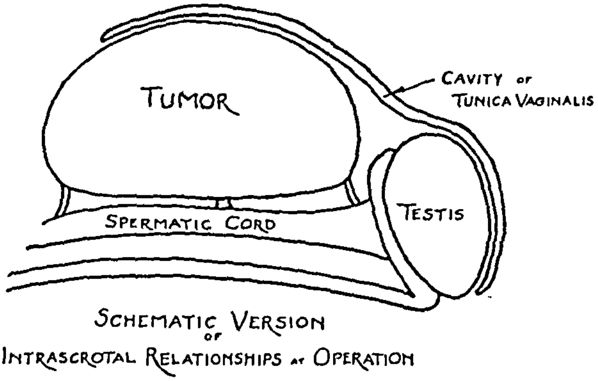
Tumor
Cavity of Tunica Vaginalis
Testis
Spermatic Cord
Schematic Version of Intrascrotal Relationships at Operation

Fig. 1

Examination revealed a well developed asthenic Negro in no distress. The patient was 74 inches tall and weighed approximately 140 lbs. Normal temperature, pulse and respirations recorded on admission. The heart and lungs were normal to routine examination. Blood pressure was 135/95. Abdominal examination revealed no abnormal masses. A firm mass, the size of an ovoid baseball, was present in the right scrotum. The mass was of rubbery consistency, nontender and roughly ovoid with an irregular surface. It did not transilluminate, was not fluctuant, was not attached to overlying skin and was situated above the testicle and epididymis and clearly differentiated from these structures. Normal spermatic cord elements were palpable above the mass to the external inguinal ring. The prostate was normal in size, shape and consistency. There was no local or generalized adenopathy.

The urinalysis on admission was essentially normal, the blood count showed mild hypochromic anemia; WBC 5,400; Kahn test negatives blood urea nitrogen

18.9 mg. per cent; phenolsulfonphthalein test showed normal function and urine culture was negative for pathogenic organisms. Chest x-ray revealed the heart and lungs to be within normal limits.

A preoperative diagnosis of tumor of the right scrotum was made.

On January 14, 1952, the right scrotum was explored. Through a linear incision the tumor was easily dissected to its attachment to the spermatic cord. The tumor was entirely outside the cavity of the tunica vaginalis and free of the testicle and epididymis. Its only attachments to the anterior aspect of the right spermatic cord were vascular. From the upper and lower poles of the tumor, small veins and their filmy connective tissue adhesions extended to the pampiniform plexus. From the spermatic cord, a small artery branched into the under surface of the mass in the approximate center of that aspect of the mass (fig. 1). At this point, the pathologist was consulted and it was the considered opinion that nothing would be gained by removing more than the tumor mass. This was easily accomplished by clamping, ligating and dividing the aforementioned vessels. The testicle, epididymis and spermatic cord were returned to the scrotum and the wound closed in layers. The patient made an uneventful postoperative recovery. He was discharged on January 28, 1952, with instructions to have periodic check-up examinations of the genitalia and abdomen.

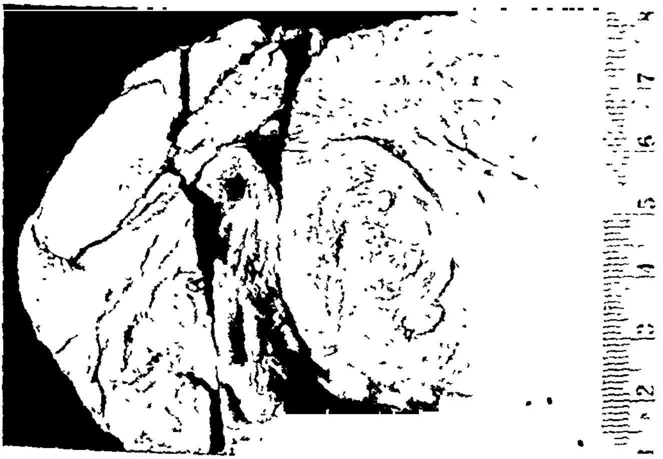

FIG. 2

Pathological report (Dr. Edward S. Cardwell, Jr., pathologist, U.S.V.A. Hospital, Columbia, S. C.): The gross specimen (fig. 2) consisted of an ovoid encapsulated mass which measures 7 by 5.5 cm. The surfaces are generally covered by loose areolar tissue except an area where there is a small amount of adipose tissue. On section, it is made up of elastic white tissue whose cut surfaces have a whorled appearance. The mass is subdivided into two parts by a fibrous capsule. One portion is ovoid and measures 5.5 by 4.0 cm. The other portion is at one pole of this and partially envelopes it. The ovoid portion is generally softer and more homogenous than the rest of the mass.

Microscopic examination of the sections of the ovoid mass reveal it to be made up of spindle-shaped cells of moderate size. They have little cytoplasm and generally there does not appear to be any intervening substance. Their nuclei are oval and vesicular. Occasional cells have large nuclei or are multinucleated. In most places, the tumor cells are very compactly arranged but in some places the arrangement is loose. Mitotic figures are present in moderate numbers. Throughout the tumor there are many large blood filled spaces which are lined either by endothelial cells or by tumor tissue (fig. 3, *A* and *B*). The other part of the tumor is made up of interlacing bundles of mature smooth muscle (fig. 3, *C* and

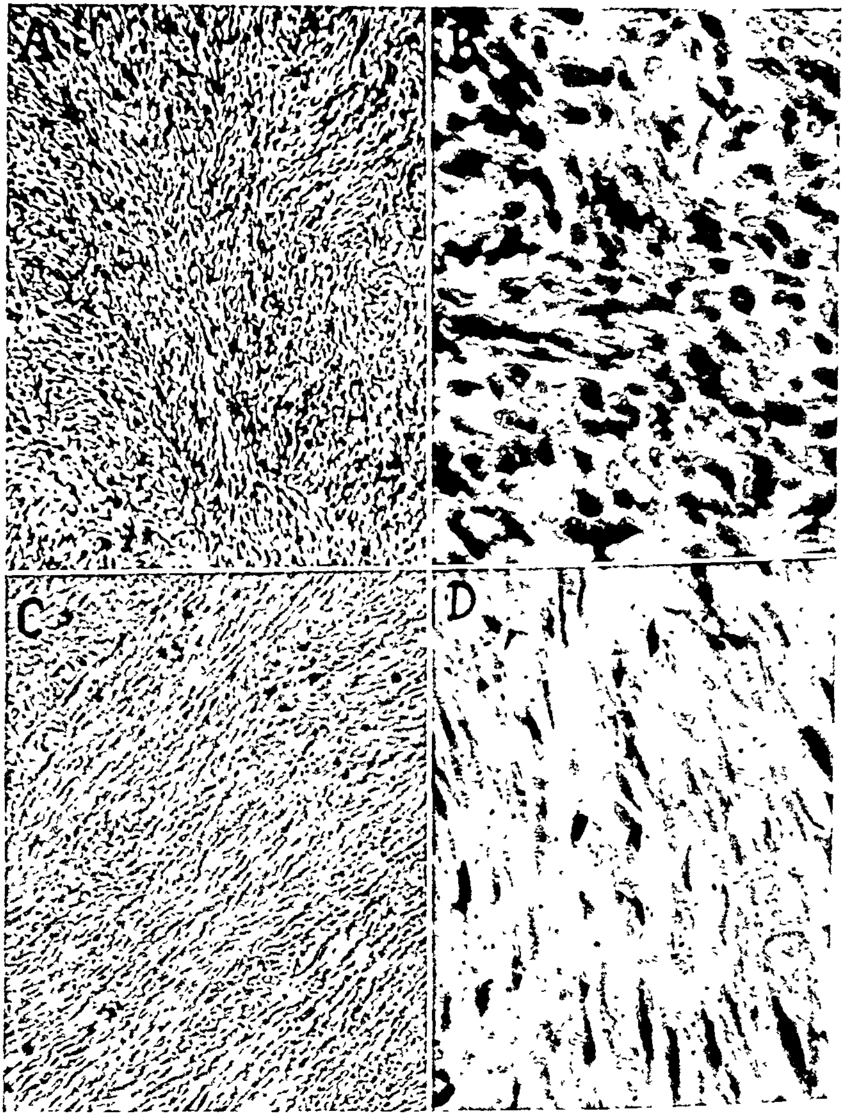

FIG. 3

D). Diagnosis: Leiomyosarcoma arising in a leiomyoma of the right spermatic cord.

DISCUSSION

Herman states that 90 per cent of extratesticular neoplasms within the scrotum occur in the spermatic cord. According to Thompson, 30 per cent of them are malignant.

Tumors of the spermatic cord are rare. Fitzpatrick, Orr, Glanton and Hayward tabulated 286 after reviewing the literature in January 1952. Sherwin and Bergman added a case (leiomyosarcoma) in February 1952.

Malignant tumors of the spermatic cord are very rare. Prince tabulated 75 in 1942. Since that time, 5 cases have been added: An embryonic carcinoma by Cole and Campagna, a rhabdomyosarcoma by Shivers, a reticulosarcoma by Perovano, a fibromyxosarcoma by McNeer, and a leiomyosarcoma by Sherwin and Bergman. Our case brings the total number of reported malignant tumors of the spermatic cord to 81.

The generally accepted classification of spermatic cord tumors is that of Hinman:

A. Benign:
  1. Epithelial (none recorded)
  2. Mesoblastic
    a. Lipoma
    b. Fibroma
    c. Myxoma
    d. Leiomyoma
    e. Vascular tumors (lymphangioma)
  3. Heterologous tumors
    a. Cystic dermoid
B. Malignant:
  1. Epithelial (no authentic cases)
  2. Mesoblastic
    a. Sarcoma (myxosarcoma, chondrosarcoma, fibrosarcoma, spindle-cell sarcoma, etc.)
  3. Heterologous tumors
    a. Teratoma (including seminoma of Chevassu)

A review of the literature adds many other types but they are mostly variations or combinations of the above classification. Only 4 cases of carcinoma of the spermatic cord have been rpeorted. Rubaschow reviewed the first 3 cases and concluded that the growths probably originated from the cell rests of the wolffian body. The fourth case is listed as an embryonic carcinoma (seminoma) by Cole and Campagna, reported by Fitzpatrick et al.

The paradox of testicular tumors having extratesticular origin and development in the cord, just as in the case of seminoma arising in the epididymis, is questionable. Piagnatti's case of epithelioma funiculi is reported as a true seminoma of the cord showing a secondary deposit in the tunica albuginea. Of the group of teratomatous tumors reported, it is probable that most of them were of sarcomatous nature.

No cases have been reported of neoplastic proliferation of the epithelium of the ductus deferens.

Tumors of the variety described in this report are considered to originate from the mesoderm. It is generally agreed that the connective tissue, the lining of the vessels, blood cells, lymphatic structures and smooth and striated muscles are derived from the mesoderm.

In this case, as in all others, trauma is thought not to play any part in the cause or development of the tumor.

It is difficult to make a clinical diagnosis of tumor of the spermatic cord. The differential diagnosis include 1) hernia; 2) hydrocele; 3) hematocele; 4) spermatocele; 5) tumor of the testes, epididymis or testicular tunics; 6) syphilis of the testis, epididymis, testicular tunics or spermatic cord; 7) tuberculosis of these structures. An exploration should be performed in the case of every mass of questionable nature within the scrotum. It is the generally accepted opinion that simple excision will suffice if the tumor is benign. It is also generally accepted that, if the tumor is malignant, the tumor, the testis, the epididymis and as much of the cord as possible should be removed and deep x-ray therapy should be given in addition. Practically all malignant tumors of the cord are sarcomas, and as few sarcomas metastasize by way of the lymphatics, the radical operation for teratoma testes, as advocated by Hinman, does not seem indicated in these cases.

The generally accepted methods of treatment were not followed in this (our) case because of the nature and position of the tumor encountered. At operation, the pathologist stated definitely that the tumor was a sarcoma. However, because of the relative isolation of the mass from the other structures, it was felt that nothing would be gained by extirpating normal scrotal contents. X-ray therapy was not given because there was no evidence of any metastases or original tumor left in the scrotum.

Very little is known about the prognosis of malignant tumors of the spermatic cord, chiefly because so few end-results of treatment have been recorded in the literature. As a rule, however, sarcomas grow rapidly and metastasize early. The slow growth of the tumor in our case is probably explained best by a consideration of the histological findings. It is postulated that, for most of its existence, the tumor was benign (a leiomyoma) and the malignancy is sarcomatous degeneration. Therefore, the prognosis in this case is good.

SUMMARY

A case of leiomyosarcoma arising in a leiomyoma of the spermatic cord is presented. The present case is the eighty-first malignant tumor of the cord to be presented and the two hundred and eighty-eighth tumor of the spermatic cord recorded.

A brief discussion of the tumors of the spermatic cord and their classification is given.

We are greatly indebted to Drs. T. M. Yates, B S. Chappell and E S Cardwell, Jr, for their opinions in this case.

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INFARCT OF THE TESTICLE: REPORT OF THREE CASES

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Infarct secondary to torsion of the spermatic cord is not a rare occurrence (Muschat and Carp),[1] but infarct of the testicle secondary to factors other than torsion is most uncommon except in the newborn. Lubash was the first to report a case in this country.[2] Cedermark reviewed 34 reported cases in 1936 and added 2 of his own.[3] Menville reported a case in 1940 in which the infarct was produced by a thrombosis which apparently originated from trauma.[4] The thrombosis occurred in the branch of the internal spermatic artery supplying the middle third of the testicle. Case reports have been made since then by Tettamante and Mainette, 1944;[5] Knudson, 1946;[6] Irazu, 1946[7] and R. de Surra Canard in 1947.[8]

Simmonds (1910) in a paper presented before the Biologic Section of the Hamburg Medical Society, was the first to emphasize the frequent occurrence of intratesticular hemorrhage in the newborn, and he regarded asphyxia as the cause of hemorrhage.[9] In his study on visceral hemorrhages in stillborn children, Spencer (1890)[10] observed intratesticular hemorrhage in 15 of 78 male children. Campbell was the first in this country to report a case of hemorrhagic infarct of the testicle in the newborn.[11] In that case the child was operated upon for tumor of the left testicle at the age of 2 months. Dry hemorrhagic gangrene was found. Subsequently, it was learned that at birth a diagnosis of bilateral hemorrhagic orchitis resulting from obstetrical trauma had been made. The frequent occurrence of intratesticular hemorrhage during birth led Halpert to routinely make gross and microscopic examination of the testicles of newborn infants.[12] In slightly over a year, among 21 male infants who died when less than one week old, 7 cases were encountered. An additional one was observed by Dr. Newbill. In 1943 MacLean reported 2 cases of hemorrhagic infarct of the testicle.[13] Both cases were diagnosed during the first week of life, and the infants were operated upon on the fourteenth and tenth day of life respectively. In 1947, Ravich reported a case which he operated on at 15 days of age.[14] The spermatic cord appeared normal and no torsion was present. The testicle and epididymis could not be differentiated and both were hemorrhagic and gangrenous.

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CASE REPORTS

Case 1. J. S., G. M. H. No. 194481, a 25 year old Negro, was seen in the general admission clinic on November 8, 1949, complaining of a vague abdominal pain that occurred between meals. It was noted on physical examination that the left testicle was 4 times normal size. It was moderately tender to palpation. On questioning, the patient stated that the swelling had been present for 3 days. He was referred to the Urology Clinic where a diagnosis of epididymitis was made, and for which he was treated. The swelling partially subsided but the remaining mass became very hard and nontender. As it remained this way and as we were suspicious that it might be a tumor of the testicle, he was admitted on January 17, 1950 for exploration of the scrotal mass.

Physical examination was essentially negative except for the left testicle which was very hard and nontender. It measured 1¼ by 1¼ by 1¾ inches. It did not transilluminate. The admission temperature was 98F, blood pressure 110 70.

Urinalyses were negative; 5.6 million red blood cells with 15.8 gm. hemoglobin, 8000 white blood cells with 48 segs, 2 stabs, 48 lymphocytes and 2 monocytes. The phenolsulfonphthalein test showed 55 per cent excretion of dye in 1 hour.

The left testicle was explored on January 18 and a biopsy was taken. The patient was discharged on January 20 with a diagnosis of chronic orchitis. As the pathological report came back "infarction of testicle," he was readmitted on February 5 for further study.

Laboratory findings on this admission were as follows: Normal urinalyses, red blood cells, hemoblogin, white blood cells and differential. Kahn negative, platelet count, bleeding time, clotting time and prothrombin time all within normal range. Sickle cell preparation was negative as was a study of the spinal fluid. An x-ray of the chest was reported as negative. An electrocardiogram was normal. Studies for tuberculosis of the urinary tract were negative. A medical consultation added nothing to our findings.

On February 3 a left orchiectomy was performed under spinal anesthesia. Report of the pathological examination by Dr. C. M. Whorton was as follows: "The gross specimen consists of a testicle, epididymis and cord submitted in the fresh state whose total weight is 15 gm. The testicle measures 3½ by 2½ by 1½ cm. in size. The color is rather dark red. The consistency is moderately firm. The epididymis is present and measures 2½ by 1 cm. in size, and at one portion has a small bluish hemorrhagic area. The cord is present, is connected with a considerable amount of tissue and measures 4 cm. in size. One microscopic section shows testis with no functioning tissue remaining. All tissue has undergone coagulation necrosis, and though the structural pattern remains, no viable cells are seen. Another section shows epididymis in which all ductile elements show varying degrees of coagulation necrosis and no viable tubule is noted. Another section shows one intact duct showing characteristic structure and cells. Diagnosis: Necrosis of testis and epididymis consistent with infarction".

The postoperative course was uneventful and the patient was discharged from the hospital on February 10.

Case 2. J. P., Jr., G. M. H. No. 391385, a 16 year old Negro, was admitted on April 12, 1950 with the chief complaint of swelling of the right testicle. He first noticed this swelling 5 days previously and denied any symptoms or signs except a mild dragging sensation in the right scrotal area. He gave no history of trauma, recent acute infection, etc. He stated that 1 year prior to admission he had experienced sudden painless swelling in the right scrotal area and that it subsided spontaneously in 24–48 hours.

Physical examination was negative except for that of the right testicle which measured 4 by 5 cm. It did not transilluminate, was very firm and nontender. Admission temperature was 98.5F and blood pressure was 120/80.

Urinalyses were negative. Red blood cells 5.3 million, hemoglobin, 13.5 gm., white blood cells 5,000 with 72 segs, and 38 lymphs. Nonprotein nitrogen 29 mg. per cent. Kahn test was negative. Spinal fluid studies were negative. Bleeding time, clotting time, prothrombin time and platelet count were within normal limits. Sickle cell preparation negative. An electrocardiogram was negative. The phenolsulfonphthalein test showed 55 per cent excretion in 1 hour. An excretory urogram and chest x-rays were negative. Studies for acid fast involvement of the genito-urinary tract were negative.

On April 4 a right inguinal incision was made, the cord isolated and a rubber shod clamp applied to it. The testicle was brought out into the operative field and examined. It was 4 to 5 times the size of the left testicle. It had a bluish discoloration and was very firm. Incision through the tunica albuginea revealed an old hematoma involving approximately 80 per cent of the testicle. In view of this, an orchiectomy was performed as a malignant condition could not be ruled out.

The report of pathologic examination by Dr. W. W. Sheldon was as follows: "The gross specimen consists of a mass of tissue which measures 4 by 4.4 by 6.5 cm. in size and is encapsulated by a thick sheet of fibrous tissue. A segment of a tissue cord measuring 4 cm. in length and 1 cm. in diameter is noted on one side opposite to which the specimen has been previously incised. On cut section, at one pole there is an encapsulated tissue mass which has the gross appearance of testicular tissue which varies from pink to reddish blue in color. The tubules string normally. The remaining tissue space is filled with clotted blood. Microscopic: Between the seminiferous tubules and tunica albuginea there are large masses of clotted blood which are undergoing autolysis. In some areas the hemorrhage is undergoing early organization from the tunica. The latter is infiltrated with a few chronic inflammatory cells. The seminiferous tubules throughout the section have undergone complete coagulation necrosis and some areas are infiltrated by polymorphonuclear leukocytes. There is one large area of hemorrhage separating seminiferous tubules. A section through the vas deferens is not unusual. In the nearly areolar tissue large blood vessels, presumably spermatic artery and vein, contain thrombi. One smaller artery has a markedly thickened intima. Diagnosis: Hematoma and infarction of testicle.

The postoperative course was uneventful and the patient was discharged from the hospital on April 19. He failed to return for a postoperative check-up.

Case 3. B. A. C., E. U. H. No. 28-127U. On January 7, 1950 this 45 year old white barber, while standing by his chair, experienced a sudden lightning-like pain that began in the area of his left costovertebral angle, radiated around the flank and into the left testicle. That evening the testicle began to swell and became very tender and painful. He had a hard shaking chill. These continued intermittently and on the following day he began experiencing frequency and dysuria. On the day of admission, January 11, he noticed gross hematuria.

Admission temperature was 104.2F, blood pressure 120/70. He appeared acutely ill and in much pain. Examination revealed moderate tenderness over the left flank area. The left testicle measured 11 by 5 by 5 cm. and was hot and very tender. It did not transilluminate.

Urinalyses: pH 5.5, specific gravity 1.017, albumin trace, red blood cells 30–40 per high power field, white blood cells 8–12 per high power field. Stain showed an occasional gram negative rod. Hemoglobin 3.0 gm., white blood cells 12 350 with 1 band, 82 segs., 15 lymphocytes and 2 monocytes. Sed. rate (Westergren) 63 mm. in 1 hour. Coagulation time 2 minutes. Kahn test was negative.

Although the temperature gradually dropped to 100F the pain remained severe so an orchiectomy was performed on January 17. The temperature returned to normal the following day and he was discharged on January 22.

In his operative note, Dr. Earl Floyd described the involved testicle as being bean shaped and measuring about 11 by 5 by 5 cm. It was dark brown in color and somewhat soft. The testicle was surrounded by a thick fibrous capsule. The spermatic cord did not appear to be involved.

The pathological report by Dr. A. Golden was as follows: "The gross specimen consists of a left testicle measuring 11 by 5 by 5 cm. and weighing 120 gm. The serosa is irregular but glistening and transmits a dark reddish grey color with many large hemorrhagic areas over the surface. The testicle is firm and slightly nodular. It is of a bean shape. On cut surface, the testicle is of a dark pinkish brown color and of soft consistency. It does not have the usual stringy appearance. The testicle is surrounded by a thick fibrous capsule. Microscopic: The sections reveal an infarction of the testicle. There is a moderate ischemic necrosis of the entire testicle with marked edema of the surrounding connective tissue. There is a moderate infiltration of polymorphonuclear leukocytes and lymphocytes in the stroma and a marked fibrosis of the capsule. No thrombosis of the blood vessels can be seen. Diagnosis: Infarction of testicle.

DISCUSSION

A review of the reported cases of infarct of the testicle, excluding the newborn and due to causes other than torsion, shows that 68 per cent occurred between the ages of 10 and 30 years. The age range was 5 to 64 years with the lesion occurring on the left side in 60 per cent of the cases. The predisposing factors include pinching and kinking of the spermatic cord, trauma to the scrotum, infection, lifting heavy objects, chilling, obstipation, and embolus and thrombus from unknown causes. Pain, swelling and tenderness are the most characteristic

Case 2. J. P., Jr., G. M. H. No. 391385, a 16 year old Negro, was admitted on April 12, 1950 with the chief complaint of swelling of the right testicle. He first noticed this swelling 5 days previously and denied any symptoms or signs except a mild dragging sensation in the right scrotal area. He gave no history of trauma, recent acute infection, etc. He stated that 1 year prior to admission he had experienced sudden painless swelling in the right scrotal area and that it subsided spontaneously in 24–48 hours.

Physical examination was negative except for that of the right testicle which measured 4 by 5 cm. It did not transilluminate, was very firm and nontender. Admission temperature was 98.5F and blood pressure was 120/80.

Urinalyses were negative. Red blood cells 5.3 million, hemoglobin, 13.5 gm., white blood cells 5,000 with 72 segs, and 38 lymphs. Nonprotein nitrogen 29 mg. per cent. Kahn test was negative. Spinal fluid studies were negative. Bleeding time, clotting time, prothrombin time and platelet count were within normal limits. Sickle cell preparation negative. An electrocardiogram was negative. The phenolsulfonphthalein test showed 55 per cent excretion in 1 hour. An excretory urogram and chest x-rays were negative. Studies for acid fast involvement of the genito-urinary tract were negative.

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DISCUSSION

A review of the reported cases of infarct of the testicle, excluding the newborn and due to causes other than torsion, shows that 68 per cent occurred between the ages of 10 and 30 years. The age range was 5 to 64 years with the lesion occurring on the left side in 60 per cent of the cases. The predisposing factors include pinching and kinking of the spermatic cord, trauma to the scrotum, infection, lifting heavy objects, chilling, obstipation, and embolus and thrombus from unknown causes. Pain, swelling and tenderness are the most characteristic signs and symptoms, although it is noted that case 1 of this report experienced only mild pain and tenderness and case 2 experienced no pain or tenderness. Usually, however, the pain is acute. The swelling and tenderness may be so marked that it is impossible to distinguish the epididymis from the testicle. The pain, swelling, and tenderness may also be noted in the spermatic cord. Hyperemia of the scrotum, fever and increased fluid in the tunica vaginalis may be present. MacLean states that there is no pain associated with hemorrhagic infarct of the testicle in the newborn, and that the patient is afebrile.

The pathological picture varies with the type of infarct and the duration of the lesion. In the acute cases of venous obstruction, the testicle is enlarged and hemorrhagic with discoloration of the adjacent tunica vaginalis. The epididymis and spermatic cord may also present this picture. Clotted blood may be present in the vessels and increased fluid may be found in the tunica vaginalis. Microscopically, necrosis of the testicle, hemorrhagic infiltration, and thrombosis of the vessels are noted. In the acute cases in which the arterial supply has been affected, the swelling of the testicle is slight. Microscopically, the picture is that of anemic necrosis. However, in some cases of arterial occlusion the tissues become edematous and permeated with blood. In the chronic cases, the testicle is destroyed by necrosis, or the parenchyma is replaced by fibrous tissue. The pathological picture, as demonstrated experimentally by Milflet[15] and also Griffiths,[16] is the result of interruption of the venous return via the spermatic vein in the presence of an intact arterial supply. In man, thrombosis of the vein secondary to torsion or direct trauma causes stasis, local anoxia, extravasation of blood, necrosis and gangrene within 48–72 hours. In the cases reviewed by Cedermark, the majority of infarcts of the testicle was produced by obstruction of the venous return. In only 1 case was there sufficient evidence to show that the testicle could be destroyed by primary obstruction of the afferent blood supply. In 2 cases testicular necrosis and histological evidence of obliterative processes in the internal spermatic artery were found, but in both, there were signs of obstruction to the venous outflow.

The diagnosis of infarct may be difficult. Torsion of the spermatic cord and orchitis may be difficult to rule out. Syphilis, tuberculosis, hydrocele, hernia, old hematocele, tumor, epididymitis, and strangulation of an embryonic appendage have to be considered before a diagnosis is made. Hernia usually gives little difficulty in diagnosis. It gives the characteristic impulse on coughing, is resonant on percussion, and when it contains bowel, gurgles on being reduced. Hydrocele has an elastic cystic feel to it, and transmits light. Acute epididymitis is invariably accompanied by severe pain and fever. Tumor of the testicle is nearly always stony hard in consistency and the diameters are often of about equal measurement. In torsion of the testicle and torsion of the appendix testis the onset of acute unilateral pain is practically always sudden. In torsion of the appendix testis there is a concomitant redness and edema of the scrotum at the onset of the attack. In cases of a few day's duration, unless edema persists, or a secondary hydrocele interferes, spot tenderness at the superior pole of the testis and just under the globus major of the epididymis is diagnostic (Randall).[17] In torsion of the testicle, Preen's sign is present whereas in hemorrhagic infarct of the testicle it is not.

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[15] Miflet, J.: Arch. f. klin. Chir., 24: 399, 1897.
[16] Griffiths, J.: J. Anat. and Physiol., 30: 81, 1895–6.

SUMMARY

A report of 3 cases of infarct of the testicle not due to torsion of the spermatic cord is presented. Two of these cases are of interest in that the onset was essentially painless. Thorough studies were made and yet the etiology was not demonstrated. A brief review of the literature is also presented.

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[17] Randall, A.: Tr. Assn. Genito-urin. Surg., 31: 283–294, 1938.

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TORSION OF THE HYDATID OF MORGAGNI

BEN E. FILLIS AND WILLARD C. MEYER

From St. Francis Hospital, Evanston, Ill.

Torsion of the hydatid is a rare clinical syndrome which, when encountered, may manifest itself as any one of several syndromes of the genito-urinary tract. The condition is of interest clinically because of its presenting complaints, and also from the embryological standpoint. Small rudimentary vestigial structures, remnants of the embryological development of the testes and the kidney, are found to cause severe pain, and at times to become incapacitating in an occasional case. A review of the embryology concerned, the anatomy as well as the literature, is presented. Two cases of torsion are presented to demonstrate the pathological anatomy as well as the therapeutic approach.

Pathological changes in the appendix testis and appendix epididymis are not encountered frequently. The subject was discussed first by Ombrédanne in 1913. Alexander Randall, in 1935, reported 73 cases, and Scott collected 85 cases which he reported in 1940. More recently, in 1945, Vermeulen and Hagerty reported 2 cases of torsion of the appendix testis. The usual disease involving the appendix testis is that of torsion, and the symptoms are those of sudden severe localized pain on the affected side radiating along the respective spermatic cord. Edema of the scrotal contents and obliteration of land marks follow quickly so that the clinical picture may be confusing. Diagnosis at this time is usually established at surgery. Epididymitis, orchitis, funiculitis and torsion of the spermatic cord enter into the differential diagnosis. Boys between the ages of 11 and 14 years are most frequently affected. Only several cases after the age of 20 have been cited.

Randall described the embryology of the sessile hydatid of Morgagni as "the most consistently present rudimentary structure of the vestigial remnants of muellerian duct origin." The structure is found on the anterior surface of the superior pole of the testes and averages 5 mm. in length. Its counterpart in the female is the appendix vesiculosa located below the fimbriated end of the fallopian tube. The appendix epididymis, which is often called the stalked hydatid, arises from a few of the cranial mesonephric tubules. The remaining tubules, according to Arey, become the efferent ductules of the epididymis, with the exception of the caudal group which remain as blind ending tubules known as the paradidymis. The appendix testis is of muellerian duct origin while the appendix epididymis is of mesonephric origin. Due to the rarity of disease involving the appendix testis, the following 2 cases merit discussion.

CASE REPORTS

Case 1. A boy aged 12 entered St. Francis Hospital, Evanston, Illinois, on April 8, 1945 complaining of recurrent attacks of right lumbar pain radiating to

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the right testicle over a period of 4 months. The attacks had occurred frequently and lasted several days. The pain was usually dull in the lumbar region, becoming severe and cramp-like in the right lower quadrant of the abdomen, with radiation to the right testicle.

On several occasions he was dismissed from classes in school during these attacks. His past history was negative except for the removal of an acute suppurative appendix at the age of ten, and one attack of pyelitis at the age of six. Physical findings were those of a healthy, somewhat obese boy. There was tenderness over both renal areas. The right seminal vesicular region was definitely tender. Both testicles were in the scrotum and the scrotal contents normal to palpation. A small left varicocele was present.

A cystoscopic survey, including retrograde urography, was performed. The urethra and bladder appeared normal except at the trigone contiguous to the right seminal vesicle, which was red and injected. All laboratory tests, including urine cultures, were normal. Retrograde urography revealed a normal upper urinary tract. He was discharged 5 days after admission, without symptoms. In discussing the findings with the patient's mother, no neurotic tendencies on the part of the boy had been observed. Eleven days later the patient was seen at the office and re-admitted to the hospital. His symptoms were more marked and in addition to the dull right lumbar pain there was a sharp, radiating pain to the right epididymo-testicular region, with definite tenderness in the area of the testicle. The spermatic cord was normal. During examination of the scrotum the patient volunteered to locate "a small, painful something that was very sore". He then manipulated a freely movable pea size mass that appeared bluish through the thin transluscent scrotal wall.

A strangulated cyst of Morgagni was removed from the right testicle the following day. The pedicle appeared about 1 cm. long and the size of a horsehair. It had been twisted through many turns. The cyst was .5 cm. in diameter, thin walled and transparent. It was filled with a cloudy, bluish-grey mucous containing numerous red blood cells. The patient recovered completely and has been symptom free.

Case 2. A 28 year old patient was referred April 5, 1946. His complaint was severe pain in the left testicle of 5 days' duration. His symptoms followed a recent series of cocktail parties. Acute epididymitis had been suspected and sulfa therapy had been given by the general doctor who first saw him. He had a history of uncomplicated gonorrheal urethritis 7 years previously. Physically he was in excellent general health and without fever. No urethral discharge was present and the urine was normal. Extreme tenderness was elicited in the left upper pole of the epididymo-testicular region. No inflammatory changes, such as redness or edema, were evident. The spermatic cord was normal, as was the prostate to palpation.

Due to the severe pain and distress the patient consented readily to enter St. Francis Hospital with the diagnosis of "torsion of the cyst of Morgagni." At surgery an incarcerated cyst was found under the pit of the epididymis and testicle about three-fourths submerged. It was about 0.7 cm. in diameter and had the appearance of a glazed fish eye. The surrounding rim of tissue was red and tense. The testicle and epididymis were otherwise normal. The cyst was dissected free, and, when ruptured, released about 1 cc of dark colored fluid under great pressure. The patient was quickly relieved of his pain.

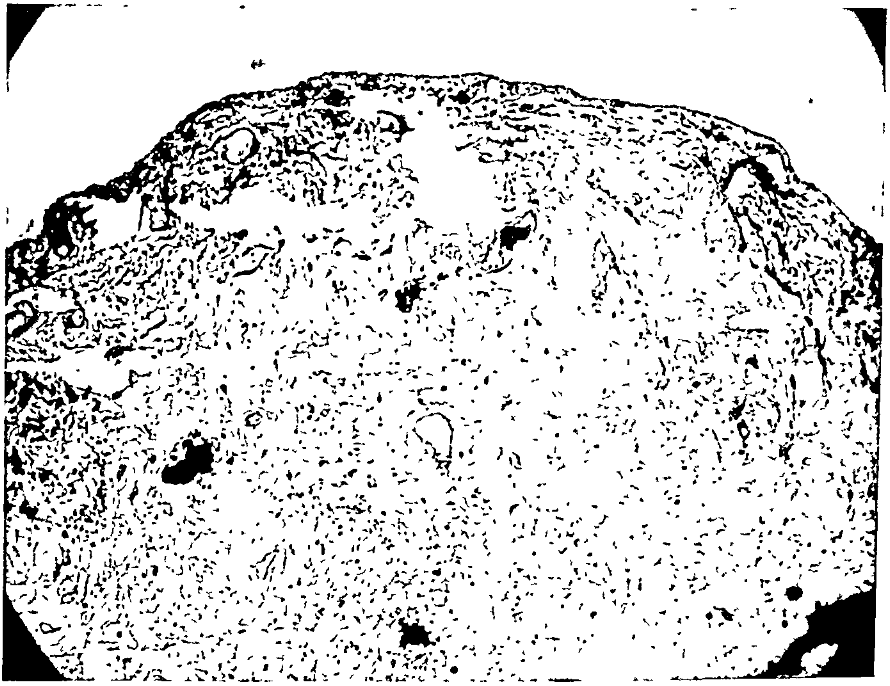

FIG. 1. Loose fibrous tissue contained in hydatid after torsion. × 130

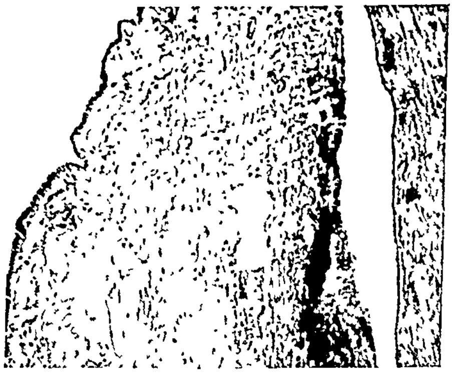

FIG. 2. Low power view of attachment of hydatid to tunica albuginea of testis. Note seminiferous tubules at lower border. × 75

MICROSCOPIC STUDY

Case 1. The specimen was made up of loose fibrous tissue with some edematous fluid seen separating the fibres. Within the stroma, occasional polymorphonuclear leukocytes were seen with a few erythrocytes noted (fig. 1). Thin walled blood vessels filled with protein, precipitate, and erythrocytes were also seen. No epithelial inclusions were seen in the stroma, as is occasionally described. Tall columnar cells usually found covering the entire structure were not seen in this case. A covering of several layers of fibrocytes which were dark staining and well differentiated was seen (figs. 2 and 3).

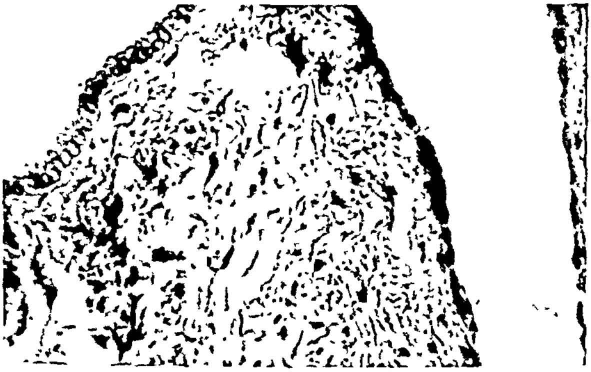

FIG. 3. High power of hydatid under torsion. Note edema of tissues. × 300

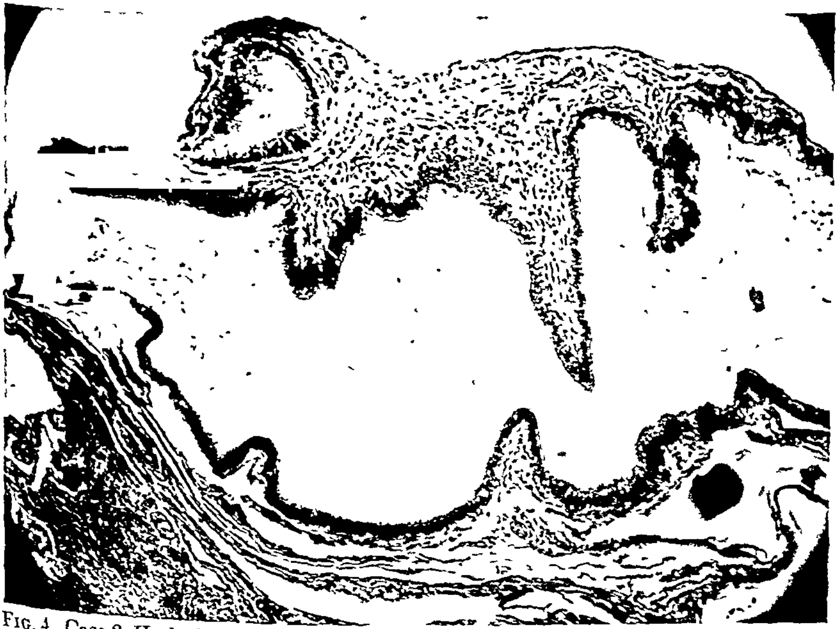

FIG. 4. Case 2. Hydatid showing infolding of epithelium of cavity lined by tall columnar ciliated cells. × 130

Case 2. Sections showed a stroma of loose fibrous tissue with lymphocytes and an occasional leukocyte. Thin walled blood vessels filled with many erythrocytes were seen. Extensive epithelial inclusions were seen with the central area of the structure being a large cavity filled with cellular debris and lined by a tall columnar ciliated epithelium. In some areas the lining of the cavity had enfolded upon itself (fig. 4), which, together with the lining epithelium, appeared not unlike the fimbriated portion of the fallopian tube. The outer covering of the cyst was devoid of an epithelial layer but appeared to be covered by a layer of fibrous tissue which was continuous with that seen in the stroma. In a recent survey of the histological structure of the appendix testis, the presence of epithelial inclusions within the stroma of the structure was found to be uncommon.

SUMMARY

Two cases of disease of the hydatid of Morgagni have been presented. Case 1 had symptoms referable to the right renal-ureteral region during a period of 4 months preceding complete strangulation. The development of the pathological condition occurred under observation and surgical intervention interrupted the usual course of inflammatory changes within the scrotum. Case 2 was unusual in that the patient's age was 28 and the cyst was incarcerated.

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RADIORESISTANT TESTIS TUMORS: RESULTS IN 133 CASES; FIVE-YEAR FOLLOW-UP

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From the Georgetown University School of Medicine, Washington, D. C.

The highly malignant tumors of the testis included in this study require a lethal tumor dose of x-rays in excess of 3000 r_v. Seminomas and benign tumors are excluded. Undifferentiated carcinoma, adenocarcinoma, papillary adenocarcinoma, trophocarcinoma and chorio-epithelioma in simple or complex form as in the so-called "Embryonal Carcinoma" grouping of Friedman and Moore[1] are the malignant elements of these tumors. Tumors of adult or mature teratoid structure with or without obvious carcinomatous elements may metastasize identically or as carcinoma and these structures resembling normal tissues are highly radioresistant.

The patients in this series were operated upon by the author or under his direction at Walter Reed General Hospital prior to July 15, 1946. Follow-up studies were conducted and all living patients in this series were examined by a group of consultants at Walter Reed Army Hospital during the years 1950–51. This restudy was made possible by the cooperation and financial backing of the National Research Council, the Veterans Administration and the staff of Walter Reed Hospital.

Statistics on the results of treatment of the total series of 250 patients are found in table 1. X-ray mortality indicates deaths from high voltage radiation incident to perforation of stomach or duodenum.

The results of treatment of 50 patients with radioresistant tumors admitted with widespread or inoperable retroperitoneal metastatic involvement are found in table 2.

The results of radical orchiectomy and million volt x-ray therapy on 55 patients with radioresistant tumors without evidence of metastasis are recorded in table 3.

The results of radical orchiectomy and million volt x-ray therapy on 28 patients with removal of retroperitoneal metastatic nodes are recorded in table 4.

The very satisfactory results obtained in the cases of seminoma are considered to be due to a highly efficient irradiation both prophylactic and therapeutic carried out under the direction of Dr. Milton Friedman of New York. We do not believe that the slightly higher rate of survival of patients with seminoma after radical orchiectomy over those treated by simple orchiectomy followed by high voltage radiation is significant. Radical orchiectomy for seminoma has given us information concerning the incidence and mode of metastatic spread and has influenced radiation techniques. Col. J. C. Kimbrough believes that radical surgery is indicated for all malignant testis tumors in the absence of widespread metastasis. We have no objection since the operation in our hands has been free of mortality and of low morbidity. In private practice patients are hospitalized for less than 10 days for radical orchiectomy.

Read at annual meeting, Mid-Atlantic Section, American Urological Association, Philadelphia, Pa., April 17, 1952.

[1] Friedman, N. B. and Moore, R. A.: Mil. Surg., 99: 573, 1946.

We are convinced that radical surgery is indicated for all malignant radioresistant tumors of the testis when preoperative studies indicate no evidence of widespread involvement. One can logically raise the question as to whether our higher survival rate for radioresistant tumors is due to the radical surgical approach or due to high voltage radiation. It is not quite fair to compare the poor results of radiation in the series of patients with widespread or inoperable metastatic involvement (table 2) with the results of radical removal of relatively small metastatic lesions in 28 patients (table 4). It should be pointed out, however, that there has been no operative mortality whereas the mortality from million volt radiation in excess of 5000 r is fairly high. We would not hesitate to recommend tumor dosage of 5000 r, for patients with retroperitoneal lymph node involvement but the prophylactic dosage of such an amount of radiation is absolutely contraindicated. Excretory or retrograde pyelographic studies will discover only the very large lesions and more particularly those on the left side.

TABLE 1

CASES	PATH DIAG	X RAY MORT	METAS MORT	LIVING
115	Seminoma	4%	7%	89%
11	Carcinoma	14%	36%	50%
33	Trophocarc.	12%	61%	27%
10	Chorioepith.	0	100%	0
66	Teratocarc.	6%	50%	44%
10	Teratoma	0	20%	80%
2	Interstitioma	0	0	100%
250		6%	34%	60%

TABLE 2

PATH DIAG	DIFFUSE METAS ORCHIECTOMY	LIVING	INOP RETRO METAS, RADICAL SURGERY	LIVING
Carcinoma	1	0	2	0
Trophocarc.	13	0	5	0
Chorioepith.	7	0	0	0
Teratocarcinoma	13	1*	9	0
	34	1	16	0

* Solitary skull metastasis removed

TABLE 3

PATH DIAG	CASES	X RAY MORT	METAS MORT	LIVING
Carcinoma	8	2	0	6
Trophocarc.	6	1	1	4
Chorioepith.	2	0	2	0
Teratocarc.	29	2	7	20
Teratoma	10	0	2	8
	55	5	12	38—69%

Therefore, it seems logical to do retroperitoneal node dissections on patients with radioresistant tumors in order to establish the presence or absence of involvement and to remove metastatic nodes.

Table 5 illustrates the findings in the 13 patients who have survived 5 years or more following orchiectomy for metastatic testis tumor.

Study of table 5 indicates that in five instances the metastatic nodes were identical with the primary tumor (trophocarcinoma). Undifferentiated carcinoma can metastasize identically or as trophocarcinoma. Teratocarcinoma can metastasize identically but usually the metastases take the form of the most malignant element, trophectoderm. The earliest microscopic metastatic lesions are usually undifferentiated carcinoma. In only 1 case in this series, however, did teratocarcinoma which showed seminoma in the primary tumor metastasize as seminoma. In other words, this one patient may have been cured by radiation following orchiectomy.

TABLE 4

PATH. DIAG.	CASES	X-RAY MORT	METAS MORT	LIVING
Carcinoma	3	0	1	2
Trophocarc.	9	3	1	5
Chorioepith.	1	0	1	0
Teratocarc.	15	2	7	6
	28	5	10	13—46%

TABLE 5

NO	TUMOR DIAG.	SIDE	METAS. NODE	SITE	IRRADIATION	LIVING
1	Teratocarc.	Rt	Trophocarc.	Precaval	3000 r$_y$	6 yrs.
2	Undif. carc.	Rt	Trophocarc.	Prerenal	4250 r$_y$	6½ yrs.
3	Teratocarc.	Rt	Trophocarc.	Precaval	5000 r$_y$	6½ yrs.
4	Trophocarc.	Lt	Trophocarc.	Prerenal	4300 r$_y$	6½ yrs.
5	Trophocarc.	Rt	Trophocarc.	Precaval	3700 r$_y$	7 yrs.
6	Teratocarc.	Rt	Trophocarc.	Precaval	2400 r$_y$	8½ yrs.
7	Undif. carc.	Lt	Undif. carc.	Comm. iliac Para-aortic 4 nodes	2600 r$_y$ 5000 r$_y$ 6000 r$_y$	5½ yrs.
8	Trophocarc.	Rt	Trophocarc.	Precaval 4 nodes	5200 r$_y$ 6200 r$_y$	7 yrs.
9	Seminoma (atypical)	Rt	Undif. carc.	Precaval 3 nodes	2000 r$_y$	8½ yrs.
10	Trophocarc.	Rt	Trophocarc.	Precaval	3600 r$_y$	6 yrs.
11	Trophocarc.	Rt	Undif. carc.	Sperm. cord	5700 r$_y$	7 yrs.
12	Teratocarc.	Rt	Seminoma	Prerenal	3900 r$_y$	6½ yrs.
13	Teratocarc.	Lt	Trophocarc.	Prerenal Para-aortic	5500 r$_y$ 5600 r$_y$	7 yrs.

It should be emphasized that in this series of cases the prerenal (nodes at or around the renal pedicle), precaval (nodes on the anterior surface of the vena cava near the entrance of the right internal spermatic vein) and para-aortic (nodes to the left of the aorta in the case of left sided tumor) nodes were involved in all instances except for one patient who had direct extension of tumor in the spermatic cord. Metastatic involvement from tumors limited to the testis proper are regularly found in the region of the renal pedicle or entrances of the internal spermatic vessels. When the tunics of the testis are involved, metastatic nodes may be found along the common and external iliac vessels. The external inguinal nodes (correctly called sub-inguinal because they lie below Poupart's ligament) are not usually involved unless the scrotum itself is involved. After radical surgery for testis tumor it should not be necessary to radiate the inguinal region. Therefore, edema of the penis, scrotum and thigh from radiation effect would be eliminated.

The effect of radiation of the retroperitoneal nodes on the adjacent structures, stomach and duodenum, and upon the spinal cord itself varies greatly with the individual. Three thousand r_v is considered "safe dosage" and sufficient for seminoma. There has been radiation gastritis with dosage of from 4000 to 5000 r to the area of the renal pedicle but when dosage of 5000 r_v or more is delivered to the retroperitoneal node area perforation of the stomach or duodenum commonly results with a high mortality. Five of our patients from whom we removed retroperitoneal metastatic nodes of highly malignant nature died from 1½ to 3 years following surgery and prophylactic radiation in excess of 5000 r_v and at autopsy there was no evidence of metastasis.

SUMMARY

Radical orchiectomy is considered indicated for all malignant testis tumors requiring more than 3000 r_v lethal tumor dosage. The lethal tumor dose for seminoma is less than 3000 r_v. It is considered better to perform the retroperitoneal node dissection and removal of the entire spermatic cord at the time of orchiectomy but there seems to be very little difference in the survival rate in the patients who have had retroperitoneal resection performed after the pathological diagnosis from simple orchiectomy is established. Biopsy of testis tumor is not considered a safe procedure. Tapping of a hydrocele to facilitate bimanual palpation of the testis may be indicated. Col. J. C. Kimbrough and his staff at Walter Reed Army Hospital and the author have performed over 300 radical resections of the retroperitoneal nodes without mortality and with remarkably low morbidity.

When there is involvement of the retroperitoneal nodes at the level of the renal pedicle, the transthoracic approach, as described by Leadbetter et al.[2] is considered best. In the absence of metastatic nodes at the renal pedicle demonstrated by means of excretory or retrograde pyelographic study, we do not routinely perform the transthoracic operation. If, however, metastatic nodes are found at the renal pedicle by the retroperitoneal route, the operation can be extended to use the transdiaphragmatic approach. Whereas complications of retroperitoneal surgery have been few, we believe that the routine use of the transthoracic approach would add considerably to morbidity and possibly to mortality. One should not hesitate to do all of the surgery that is necessary to cure these young men of malignancy.

915—19th St. N.W., Washington 6, D. C.

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[2] Leadbetter, W. F., Feeley, J. R. and Wheeler, J. S.: Urol. Survey, 1: 447, 1951.

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A MALIGNANT TESTIS TUMOR WITH HEPATIC METASTASIS IN A GRIZZLY BEAR

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From the James Buchanan Brady Urological Institute, and the Department of Pathology, The Johns Hopkins Hospital, Baltimore

Spontaneous malignant testis tumors in domestic animals are not rare.[1, 2, 3, 4] However, Fox found no mammalian testis tumors in 1,860 autopsies on captive *wild* animals dying in the Philadelphia Zoological Garden.[5] So far as we know there are no previous reports of testis tumors in bears, although on the basis of the common origin[6] of the bear and the dog (in which they occur not infrequently) they might be expected to occur.

An aged and infirm grizzly bear died suddenly in the Baltimore Zoo.[7] He was said to be 34 years old and had been sick for over a year. There was no gross evidence of gynecomastia nor history of sexual precocity. A partial autopsy was performed 24 hours after his death.

The bowel was full of pinworms. There was a large tumor of the left testis surrounded by a dense fibrous capsule (fig. 1). The right testis was atrophic. The rest of the urinary and genital tract was normal. The prostate was small and firm. The liver contained a large well-encapsulated solitary metastasis (fig. 2).

On section the testis tumor was yellowish-brown, very firm and in some areas there was calcification. There were many cystic areas. Grossly the appearance suggested a teratoma. The liver metastasis was whitish-yellow and quite firm throughout.

The pathologist's report (S.P. No. 51-1508) is as follows: "The gross specimen of liver shows a large segment replaced by a rounded nodule of metastatic tumor which measures about 10 cm. in diameter. It is white and firm. One testis is replaced by a large mass measuring about 10 by 6 by 6 cm. and surrounded by a dense connective tissue capsule, with the cut surface showing irregular areas of firm white tissue interspersed with other areas of cystic and hemorrhagic change with much calcification.

"Microscopic: The testicular tumor assumes varying degrees of anaplasia. The marked cellularity is interrupted by areas of necrosis, hemorrhage, and broad bands of hyaline connective tissue. Where the cells are best differentiated they are large and polygonal with abundant pink cytoplasm and small round

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[1] Feldman, W. H.: Neoplasms of domesticated animals. (Mayo Clinic Monographs), p. 76. Philadelphia: W. B. Saunders Co., 1932.

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[5] Fox, H.: Disease in captive wild mammals and birds. Philadelphia: J. B. Lippincott Co., 1923.

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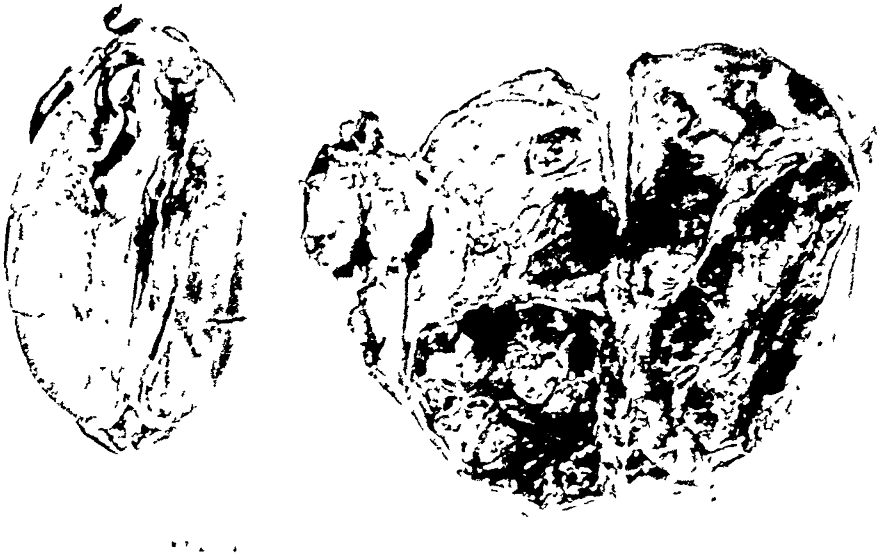

FIG. 1 Large tumor of left testis surrounded by dense fibrous capsule (right above). Right testis was atrophic.

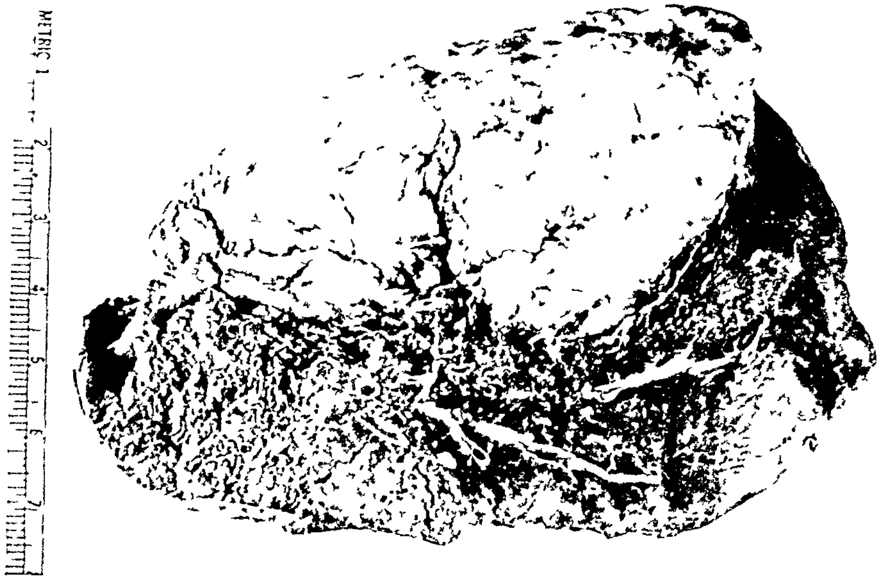

FIG. 2. Liver contained a large well-encapsulated solitary metastasis

nuclei. Very fine yellowish-brown pigment granules, which do not take a positive Prussian blue reaction, are contained within many of these cells, and thus they resemble interstitial or Leydig cells. There are transitional stages between this cell type and the abundant anaplastic cells, which have small dark round nuclei and little or no cytoplasm. In many areas irregular columns of these cells are separated by bands of hyaline connective tissue (fig. 3, *A*). The liver nodule consists entirely of tumor of this anaplastic type, with much necrosis, but clearly represents a metastatic focus (fig. 3, *B*). Diagnosis: Malignant interstitial cell tumor of testis, with metastases to liver."

Sections of the prostate, normal testis, kidney and adrenal were not remarkable.

Dr. Arnold Rich (Department of Pathology) kindly reviewed the sections. He felt that, despite the pleomorphism and irregularity of many of the cell types, there were many areas containing malignant cells which looked like interstitial cells. He observed that the microscopic picture was compatible with that of malignant interstitial cell tumor.

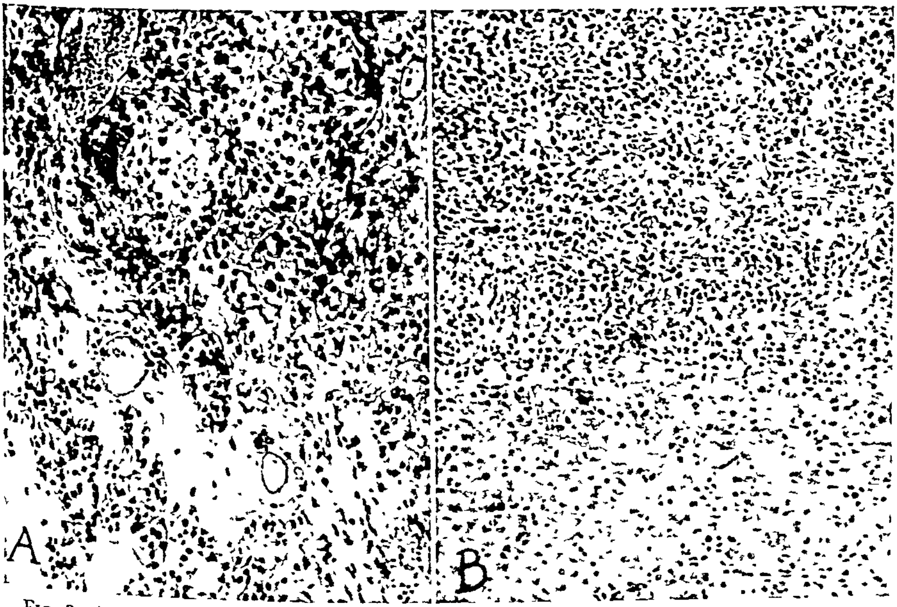

FIG. 3. *A*, testicular tumor showing many of the larger polyhedral interstitial cells. Also present are areas of hyaline connective tissue with smaller anaplastic cells throughout. *B*, liver metastasis showing remaining parenchyma, bottom, with metastatic tumor composed of small anaplastic cells. (× 150)

Sections of the primary tumor and the metastasis were sent to Professor R. A. Willis of Leeds, an authority on animal tumors. His response was as follows:[8] "The tumour is clearly a highly cellular and malignant one, so that it is not surprising that in many parts it is not easy to identify. However, in some parts of the testicular growth the cells are large and polyhedral, and contain intracellular brown pigment, and I have no doubt that these are of the nature of interstitial cells. Since all transitions can be traced between these and the more anaplastic cells, I believe the growth to be a malignant interstitial-cell tumour. Another structural point favouring this diagnosis is the way in which ramifying trabeculae of tumour cells are separated in places by a hyaline connective tissue, a type of structure which is not uncommon in interstitial-cell tumours. The fact that the bear is closely related to the dog again supports this diagnosis, since the interstitial-cell tumours are quite common in the dog. I feel sure that the tumour is not a seminoma, and there is certainly no evidence in the sections which you sent to suggest that it is a teratoma.

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[8] Willis, R. A.: Personal communication.

"The tumour in the liver is, I think, undoubtedly a metastasis from the testicular tumour."

DISCUSSION

Although interstitial cell tumors of the testis are rare in humans[9,10] they are apparently quite common in the dog.[2] The common ancestry of bears and dogs[6] would suggest that bears might also frequently suffer with this type of tumor, although it is not previously reported. Interstitial cell tumors in humans are commonly associated with sexual precocity and/or gynecomastia.[10] This is not reported in animals and was not observed in this case. Most animal interstitial cell tumors have been reported in old dogs. The bear reported here was very old, approaching the limit of reported age for bears in captivity (35 years). Speculation may arise as to whether or not the interstitial cell tumors in aged animals are comparable with those in young humans even though they are apparently of the same tissue origin.

SUMMARY

A malignant testis tumor, probably originating in the interstitial cells, with metastasis to the liver, is reported because of its occurrence in an aged captive grizzly bear. It is compared with similar tumors reported in old dogs on the basis of the common ancestry of the bear and the dog.

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UROKON SODIUM 70 PER CENT IN EXCRETORY UROGRAPHY

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An ideal contrast medium for urography must be fluid, composed of inert nontoxic material, which injected intravenously will be nonirritating to tissue, have a low osmotic pressure, give a high contrast, and be rapidly and entirely excreted in a reasonable time, leaving no ill effects. We have had heretofore solutions which almost entirely met these criteria, but we still had a large percentage of incompletely filled pyelograms which were not surgically diagnostic. This is in part due to continued peristalsis by the renal drainage system and in great part to an insufficient concentration of the contrast medium. The present paper reports the use of a more concentrated solution (70 per cent) of Urokon in over one thousand cases. Analysis of the observations leads to the conclusion that the higher dosage used increases two-fold the percentage of diagnostic intravenous pyelograms while producing fewer untoward effects than previous studies would indicate.

In 1950, the Mallinckrodt Chemical Works introduced Urokon® Sodium (Sodium 3-acetylamino-2,4,6-triiodobenzoate or Sodium acetrizoate). Since its inception it has been widely accepted and several papers have compared it with other accepted media and offered suggestions for its use to obtain best results.

Robbins, Colby et al.[1] compared 30 per cent Urokon with 35 per cent Diodrast. They concluded that in general the densities of the media were equal, but excretion of Urokon more rapid. The diagnostic quality of the films were of the same order. They were impressed by the low incidence of vasomotor response to Urokon. Nesbit and Lapides[2] reported examinations employing 50 per cent Urokon in 400 patients and 30 per cent Urokon in 1021 patients. They suggested that an optimum of 90 seconds be allowed for injection. Their conclusions were that there was no essential difference in the quality of the pyelograms as produced by Urokon in its recommended dosage of 25 cc of the 30 per cent solution, Diodrast 20 cc of 35 per cent, and Neo-Iopax 30 cc of 50 per cent. They reported the most common reactions as follows: nausea and [illegible] with Urokon; nausea and vasomotor reaction with Diodrast, and [illegible] arm pain with Neo-Iopax.

Richardson and Rose compared 30 per cent Urokon with 50 per cent [illegible]

Accepted for publication July [illegible], 1952

[1] Robbins, [illegible], Colby, F. H., Thomas, [illegible] and Joyce, [illegible]: [illegible] A clinical trial of a new contrast medium [illegible] Radiology, [illegible], 1952.

[2] Nesbit, R. M. and Lapides, J.: [illegible] Urokon [illegible] medium [illegible] 1951.

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[4] Richardson, [illegible] and Rose, D. K.: [illegible] Urokon [illegible] J. Urol., [illegible] 1952.

Iopax. They concluded that the pyelograms when Urokon was used gave greater contrast. Urokon pyelograms appeared earlier and disappeared more rapidly than those with Neo-Iopax. With each medium 33 per cent of the "nonsurgical" cases were inadequate. In those cases where surgery was contemplated, 72 per cent with Urokon and 74 per cent with Neo-Iopax were inadequate. Those pyelograms made with Neo-Iopax were in general more completely filled in an individual film and the calyceal and ureteral collecting systems appeared more relaxed. At the very rapid rates of injection, Urokon pyelograms were much too sketchy in total visualization even using all films. This hypermotility could be controlled by slow injection of the medium. They recommended that the rate of injection of Urokon should be optimally four minutes. A rapid rate of injection predisposed to a greater number of side reactions, but the more rapid the injection the more opaque was the pyelographic shadow.

Wall and Rose[5] in presenting intravenous nephrography not only described a simple method for brilliant outlining of the renal shadow but demonstrated repeatedly completely filled pyelo-ureterograms following the rapid injection of 50 cc of 70 per cent Urokon. They stated: "Comparisons with routine excretory urograms on the same patients suggest that the present dosage in use for excretory urography does not provide the maximum amount of contrast medium that can be utilized by the kidney." This observation led to the present investigation of 70 per cent Urokon in routine pyelography.

In this paper are embodied the results of that investigation in 1160 consecutive cases of routine pyelography employing varying amounts of 70 per cent Urokon.*

TECHNIQUE

The patients were prepared for excretory urography. All patients were dehydrated. The vast majority, both hospital and out-patients, received cathartics as well. Castor oil 30 cc or milk of magnesia and cascara in varying proportions (30:4 cc or 20:10 cc) were employed. The best preparations were consistently obtained with castor oil 30 cc administered after the evening meal. The routine flat film was taken on standard urographic tables for correction of technique and comparison with following pyelograms. The patients were asked about previous allergic phenomena and where indicated skin tests for sensitivity accomplished. The medium was then injected from an ordinary 50 cc Luer Lok syringe through needles ranging in gauge from 20 to 18. The time of injection was as rapid as ordinary effort permitted through the needle in use. Almost all injections were completed within 15–20 seconds. Film exposures in adults were made at 5, 10, and 15 minutes with an erect film immediately following the 15 minute flat film. Delayed exposures were made when conditions so indicated. Due to the more rapid excretion in children, the first film was made at 3 minutes following completion of injection with subsequent pyelograms at 8 and 12 minutes.

[5] Wall, B. and Rose, D. K.: The clinical intravenous nephrogram: Preliminary report. J. Urol., **66**: 305–314, 1951.

* The medium as well as energetic assistance was furnished by Dr. Melvin A. Thorpe of the Mallinckrodt Chemical Works.

QUALITY OF PYELOGRAMS

The standard adopted for grading the pyelograms was based on that contrast and filling which are obtained in a well filled retrograde pyelogram. Such pyelograms are of surgical diagnostic quality. The films were graded accordingly in decreasing quality from 1 to IV with 1 considered equivalent to a perfect retrograde filling. In the large group of cases presented several observers at the daily combined radiological-urological staff conference took part in the grading; so an unbiased opinion is more nearly presented. Grade IV represents nonvisualization even on reasonably delayed films and represents many patients who because of extreme renal damage or azotemia should never have had excretory pyelograms in the first place. After reviewing the cases, the division between diagnostic and non-diagnostic films falls between grades II and II−, as seen in table 1.

TABLE 1. *Quality of pyelogram*

GRADE	NUMBER
I	55
I−	326
II+	79
II	273
II−	167
III+	11
III	177
III−	44
IV	28
Total	1160

Of the 1160 cases reported, consecutive cases executed by both the radiological and urological departments, there are represented all types requiring excretory urography as an aid to diagnosis and therapy. It may be seen that 407 cases or 35 per cent were not diagnostic; that is, were not well filled enough to satisfy criteria for purposes of surgical intervention. It is felt that these standards are more rigid than customarily employed in papers dealing with this subject but are justifiable. We further believe that our 62 per cent of surgically diagnostic excretory pyelograms is by far better than heretofore obtained with any other intravenous contrast medium. The density is quite noticeably greater and the pyelograms thereby clearer and brighter. In those well-filled, the entire pelvis in simultaneous filling phase, and those broken into filled segments due to peristalsis of the calyces, infundibula, and pelvis, we find this increased density of great diagnostic value, particularly in the latter where a complete pyelogram must be pieced together.

In this study we have continued the investigation of the value of pressure binders in excretory urography where they were not contraindicated by preexisting [illegible] or [illegible] obstruction.

Table 2 summarizes our findings in the [illegible] cases where the use of [illegible] was

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Wall and Rose[5] in presenting intravenous nephrography not only described a simple method for brilliant outlining of the renal shadow but demonstrated repeatedly completely filled pyelo-ureterograms following the rapid injection of 50 cc of 70 per cent Urokon. They stated: "Comparisons with routine excretory urograms on the same patients suggest that the present dosage in use for excretory urography does not provide the maximum amount of contrast medium that can be utilized by the kidney." This observation led to the present investigation of 70 per cent Urokon in routine pyelography.

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In this study we have continued the investigation of the value of pressure blocks in excretory urography where they were not contra-indicated by pre-existing intrinsic or extrinsic obstruction.

Table 2 summarizes our findings in the 937 cases where the use of blocks was or was not indicated. It is significant to note that about 10 per cent more cases are diagnostic when blocks are used.

DOSAGE

In this paper there are included 142 cases in which 50 cc of 70 per cent Urokon was injected. Of this group 73 per cent were diagnostic. A very significant and convincing argument in favor of increased amount and concentration of medium is readily apparent when the results of 36 pyelograms in children 16 years and under are analyzed. Twenty-five were under 10 years. All under 4 years of age received 12–15 cc. Those 6 years of age and above received 25 cc except two. One of these received 15 cc, and the other, a girl of 15 with a congenital absence of one kidney and 8 years postoperative from ureterosigmoidostomy, received 50 cc of 70 per cent Urokon. The latter had no reaction beyond the usual taste and flush. The youngest child, 2½ months, received 12 cc. Of this group, 86 per cent were surgically diagnostic.

TABLE 2. *Use of compression blocks*

	DIAGNOSTIC		NON-DIAGNOSTIC	
	with blocks	without blocks	with blocks	without blocks
Number	207	365	104	261
Per cent	66½%	58%	33%	42%

TABLE 3. *Best filling pyelogram*

TIME	MINUTES								HOURS			OTHERS	TOTAL
	5	10	15	15E	20	25	30	45	1	2	3		
Number	376	335	240	8	10	7	20	3	19	5	1	1	1025

TABLE 4. *Urokon recovery from urine after injection of 50 cc of 70 per cent Urokon (35 gm.)*

	0–6 HOURS	6–12 HOURS	12–18 HOURS	18–24 HOURS	24–30 HOURS	TOTAL
Case 1	—	—	—	—	—	93.8%
Case 2	—	—	—	—	—	90.0%
Case 3	82.8%	4.7%	1.5%	0.5%	—	89.5%
Case 4	58.5%	17.0%	5.2%	2.5%	0.4%	83.6%
Case 5	88.2%	4.5%	1.0%	0.0%	—	93.7%

EXCRETION OF THE MEDIUM

It has been stated by all observers that Urokon is the most rapidly excreted of all the commonly employed contrast media. This is most graphically presented in table 3, which lists the film time demonstrating the best filling pyelogram. In 1025 cases where this observation was noted, 951 or 92.8 per cent filled within 15 minutes. Delayed filling, of course, occurred almost without exception where partial urinary obstruction existed. In a busy clinic or office the rapidity with which the medium is concentrated should be of prime importance.

Urokon is not decomposed in vivo, and is excreted unchanged.[6] Urokon recovery studies were made* on total 24 hour urine specimens following intravenous nephrography where 50 cc of 70 per cent Urokon (35 gm.) was injected in 5 patients. In 2 cases only the total excretion was measured, these being 93.8 per cent and 90 per cent respectively. The other 3 cases were divided into 6 hours increments. Reference to table 4 and figure 1 reveals that the vast majority of the medium is recovered in the first 6 hour specimen.

Wall and Rose[4] previously reported that 50 cc of 70 per cent Urokon educed biliary elimination of the medium, occasionally affording excellent gallbladder shadows in patients with poor renal function. Considering this fact in addition to the loss of medium in transfer from ampule to syringe, to patient, this is remarkable excretion recovery.

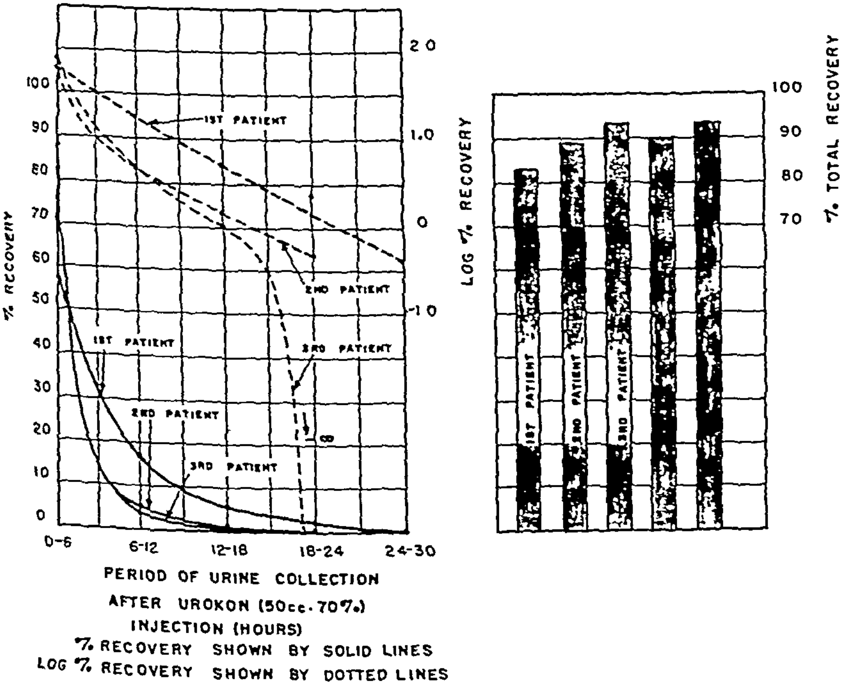

FIG. 1

REACTIONS TO INJECTION

In the tabulation of this large series of cases, the observers became lax in recording the presence or absence of reactions because of the marked absence of toxic reactions. For this reason, only 556 of the total are so noted. Of this group 497 or 89.5 per cent had no reaction. The majority of the patients experi-

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[6] Neuhaus, D. R., Christman, A. A. and Lewis, H. B.: Biochemical studies on Urokon, a new pyelographic medium. J. Lab. & Clin. Med., 35: 43–49, 1950.

* Urokon recovery studies were conducted by Dr. W. R. Armstrong and Miss Darline Hilker of the Mallinckrodt Chemical Works laboratories.

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Case 3	82.8%	4.7%	1.5%	0.5%	—	89.5%
Case 4	58.5%	17.0%	5.2%	2.5%	0.4%	83.6%
Case 5	88.2%	4.5%	1.0%	0.0%	—	93.7%

One of these received 15 cc, and the other, a girl of 15 with a congenital absence of one kidney and 8 years postoperative from ureterosigmoidostomy, received 50 cc of 70 per cent Urokon. The latter had no reaction beyond the usual taste and flush. The youngest child, 2½ months, received 12 cc. Of this group, 86 per cent were surgically diagnostic.

EXCRETION OF THE MEDIUM

It has been stated by all observers that Urokon is the most rapidly excreted of all the commonly employed contrast media. This is most graphically presented in table 3, which lists the film time demonstrating the best filling pyelogram. In 1025 cases where this observation was noted, 951 or 92.8 per cent filled within 15 minutes. Delayed filling, of course, occurred almost without exception where partial urinary obstruction existed. In a busy clinic or office the rapidity with which the medium is concentrated should be of prime importance

Urokon is not decomposed in vivo, and is excreted unchanged.[6] Urokon recovery studies were made* on total 24 hour urine specimens following intravenous nephrography where 50 cc of 70 per cent Urokon (35 gm.) was injected in 5 patients. In 2 cases only the total excretion was measured, these being 93.8 per cent and 90 per cent respectively. The other 3 cases were divided into 6 hours increments. Reference to table 4 and figure 1 reveals that the vast majority of the medium is recovered in the first 6 hour specimen.

Wall and Rose[4] previously reported that 50 cc of 70 per cent Urokon educed biliary elimination of the medium, occasionally affording excellent gallbladder shadows in patients with poor renal function. Considering this fact in addition to the loss of medium in transfer from ampule to syringe, to patient, this is remarkable excretion recovery.

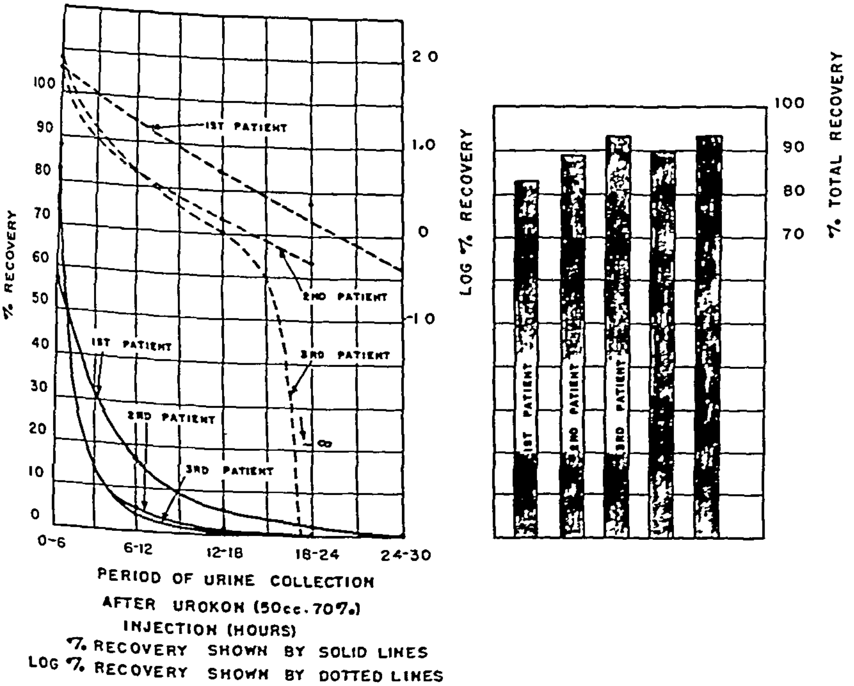

FIG. 1

REACTIONS TO INJECTION

In the tabulation of this large series of cases, the observers became lax in recording the presence or absence of reactions because of the marked absence of toxic reactions. For this reason, only 556 of the total are so noted. Of this group 497 or 89.5 per cent had no reaction. The majority of the patients experi-

[6] Neuhaus, D. R., Christman, A. A., and Lewis, H. B.: Biochemical studies on Urokon, a new pyelographic medium. J. Lab. & Clin. Med., 35: 43-49, 1950.

* Urokon recovery studies were conducted by Dr. W. R. Armstrong and Miss Darline Hilker of the Mallinckrodt Chemical Works laboratories.

enced a very transient foreign taste described as bitter or metallic. A like number experienced a minimal flush in the blush area, rapid in onset, and fleeting in duration. Neither taste nor flush were considered as reactions (except where flush was marked as noted in table 5) because of the very minimal response. Of the sum total, it is our impression that the percentage would vary toward a greater number without reaction. Notation of a reaction is more likely to occur than the contrary since it is forcibly brought to the attention of the observer. We realize that this is at variance with previous authors,[2, 3, 4] who would have predicted a greater tendency to reaction from their findings on slow injection and recommended dosage. We are at a loss to explain much of it, but suffice it to say, the results speak for themselves.

TABLE 5. *Reactions*

	CASE
No reaction	497
Nausea with emesis	21
Flush (marked)	13
Nausea	10
Urticaria	4
Cough	2
Sneeze	2
Pain in shoulder	2
Severe reaction	2
Headache	1
Respiratory difficulty	1
Palpitation of heart	1
Total	556

Table 5 presents the reactions noted. There were 2 patients who presented rather troublesome reactions, both of whom had nausea with emesis, fecal incontinence and drop in blood pressure to shock levels. Both made prompt recoveries with symptomatic and supportive therapy.

Nausea and nausea and emesis, when they occurred, were early and fleeting, appearing within 1 minute from the onset of injection and clearing within 3 minutes from onset of injection. There have been no lasting reactions. Urticaria occurred in 4 cases and with one exception cleared promptly after intravenous Benadryl (2–3 cc). It is the impression of the authors that much of the nausea ascribed to excretory urography is psychic in a fearful patient, who may not feel well after catharsis the night before. We have injected 25 cc of 30 per cent Urokon rapidly in a significant number without reaction; although it is also our impression that nausea and nausea with emesis are more common with the use of 30 per cent Urokon. The observation of Seevers referred to by Richardson and Rose[4] that Urokon acts as a central emetic drug producing vomiting and the prediction that if the drug is injected very rapidly the plasma concentration may reach a level which will stimulate the vomiting mechanism, may not then be borne out unless the larger dose overwhelms the center. Seevers[7] believes that this is not likely for this type of compound. The same authors state that the hypermotility thought to be increased by very rapid rates of injection can be controlled by slow injection. We now believe that this is not true and that the so-called "hypermotility" so often seen in the hypertensive patient with a "spidery" pelvis is due to some not yet known intrinsic factor, which so far has escaped control.

It has also been noted repeatedly that after a 50 cc injection of 70 per cent Urokon the immediate urine sample shows a shower of epithelial cells which some observers have thought resembled tubular cells. The percentage which show this reaction is not known but the impression is about 50 per cent. Still another group receiving 50 cc of 70 per cent have shown transient albuminuria (trace to 1+ by heat coagulation). They represent a much lower percentage and the albuminuria has been absent on the following day in ten such cases that were followed. Further investigation on these two observations is now being carried on and will be reported at a later date. After a little over one year's experience, no permanent injury has been noted in any patient receiving 70 per cent Urokon.

Local spills cause immediate pain, and if any notable amount is spilled, it has been found judicious to inject hyaluronidase into the local area with gratifying results. Prior to the use of hyaluronidase sizable spills resulted in discomfort for 24–72 hours and the healing process left considerable fibrosis. Some half dozen cases of antecubital vein phlebitis have occurred and these mostly in the summer months.

SUMMARY AND CONCLUSIONS

Instrumental manipulation of the urinary tract should not be performed other than such as is necessary to arrive at an accurate diagnosis. Retrograde pyelograms often may be complimentary to intravenous pyelograms. Toward this end, the authors present a preliminary report on the use of 70 per cent Urokon in routine excretory urography. Salient features are:

Greater density and higher contrast are obtained with 70 per cent Urokon than with any other intravenous medium.

Surgically diagnostic pyelograms are increased to 62 per cent in adults and to 86 per cent in children.

More rapid excretion and hence shorter examination time per patient.

Greatly decreased toxic reaction over that of any other medium now employed.

Slow injection rate not necessary nor desirable.

3720 Washington Blvd., St. Louis 8, Mo.

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[7] Seevers, M. H., Personal communication.

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